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THE LESSER ELECTROCARDIOGRAPHIC SIGNS OF CARDIAC PAIN

BY

WILLIAM EVANS AND COLIN McRAE*

From the Cardiac Department of the London Hospital

Received March 20, 1952

When the cardiographic diagnosis of cardiac infarction was first described a characteristic pattern was assigned to the pathological tracing; it consisted of deviation of the S–T segment, inversion of the T wave, and often the presence of significant Q waves (Herrick, 1919; Pardee, 1920; Parkinson and Bedford, 1928). The next few years saw a search for leads that would portray the lesser changes of myocardial injury more clearly than the orthodox limb leads, and so chest lead electrocardiography came into use (Wolferth and Wood, 1932).

Among patients with a characteristic history of cardiac pain there continue to be many in whom the cardiogram appears to be normal on casual examination. Closer scrutiny of such tracings frequently shows changes that, although small, do not tally strictly with the slight variants found in a tracing traditionally accepted as physiological.

We determined to examine such changes more closely and especially to watch the progress of patients exhibiting them, in order to apportion to each its true significance, and to test their value in the diagnosis of cardiac pain.

Some eight changes meriting such assessment came to our notice and they include the presence of a wave in the P–Q period, notching of the QRS complex, addition of an R1 wave, depression of the S–T segment, a low T wave, a blunt T wave, terminal dipping of the T wave, and an inverted U wave.

In the investigation of each cardiographic sign the same procedure was followed. The electrocardiograms were recorded deliberately with three machines (Cambridge, Elmqvist, and Sanborn) lest a slight change might be an instrumental artefact. Leads I, II, III, CR1, CR4, and CR7 were recorded in all cases while III R, intermediate bipolar chest leads, and V leads were taken in the majority. The tracings from 156 healthy subjects were first examined to determine whether a particular sign might be a normal variant. If it was absent in the healthy group it was then sought in the tracings from patients in whom there was a characteristic history of cardiac pain but an electrocardiogram that had previously been regarded as normal. Whenever one of the lesser cardiographic signs was present in these patients, other evidence was sought to give proof that their symptom was true cardiac pain. Such evidence was considered to be present if a one-time physiological cardiogram had been recorded fortuitously when chest pain was not a symptom, if a previous or subsequent tracing had shown undisputed changes of cardiac infarction, if cardiac anoxæmia following physical exercise had produced cardiographic changes accepted as typifying cardiac ischæmia (Masters *et al.*, 1942; Wood *et al.*, 1950), or if death had occurred unexpectedly from cardiac infarction and before an opportunity had presented to test the significance of the cardiographic sign. These minor electrocardiographic changes will now be discussed in turn.

A Wave in the P–Q Period

When a small upright deflection is found in the final phase of the P–Q period it appears to be part of the QRS complex, but it can hardly be designated an R wave because the downward deflec-

* Holding a grant from the Research Fund of the Royal Australasian College of Physicians.

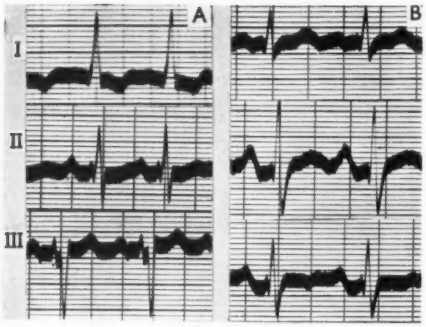

FIG. 1.—A wave in the P–Q period. A short pointed wave appears before the primary R wave in leads II and III. (A) is from a patient with aortic incompetence and (B) from a healthy subject.

tion that may immediately follow it is undoubtedly a Q and not an S wave. In most of the cases in which we have identified the wave the P–R period has not been long enough to allow an auricular T wave to appear, nor has it the same form, being much more pointed than the Ta wave. Again, when this wave appeared earlier in the P–R period it has never seemed an integral part of the P wave itself, while its appearance in auricular fibrillation confirms that it is independent of the P wave. Although we found this wave, seldom measuring more than 1 mm. in height, in patients with thyrogenic, hypertensive, and coronary artery disease, and in those with bundle branch block, we sometimes found it in our series of healthy subjects (Fig. 1). We were able to conclude that the presence of this wave in the P–Q period of the cardiogram of a patient subject to chest pain does not indicate a myocardial injury.

NOTCHING OF THE QRS COMPLEX

According to the New York Heart Association (1940) a deflection is slurred if one of its limbs or its peak shows an obvious local thickening; the term should not be applied to the slight thickening at the apex of the wave or just where it leaves or returns to the base-line. A notched deflection is characterized by spikes on one or other of its limbs, while a splintered deflection is one which shows two or more apices. We believe that all three changes reflect the same mechanism, namely an interruption in the progress of the electrical impulse through the myocardium and that the distinction between them is one of degree only. If an apparent slur is examined under magnification it will often be seen as a minute notch. We have found it more convenient to refer to all three changes as *notching* and to designate the grades of notching as slight, moderate, or prominent.

The relationship of notching of the QRS complex to myocardial damage has been discussed in the past (Carter, 1914 and 1918; Wedd, 1919; Wilson and Herrmann, 1920). The New York Heart Association stated that slurring, notching, or splintering of the QRS was abnormal if it appeared in two leads and nearer the peak than the base in one of them. Bayley (1946) stated that such changes usually, although not invariably, indicated death of a portion of the myocardium. In 95 patients in whom patchy fibrosis of the myocardium was found at necropsy, Weinberg *et al.* (1950) reported notching of the QRS in 32 per cent, but without specifying the affected leads; they stated that notching, other than in lead III, was almost invariably a sign of myocardial damage and they emphasized a statement made before by one of them (Katz, 1946) that notching was more likely to be significant if it happened nearer the apex than the base of the complex, was present in multiple leads, and was obvious. It had no significance if the change was slight or was associated with a tracing of low voltage.

Notching of the QRS in lead III was common in our healthy series and was found in more than one-third of the 156 cases. On the other hand, notching in leads I and II is uncommon, 11 and 13 among 2000 cases (Hall *et al.*, 1942), 13 and 4 among 500 cases (Stewart and Manning, 1944), and 23 and 35 among 1000 cases (Graybiel *et al.*, 1944). In our series (see Table I) prominent notching in leads I and II was never met with either alone or in combination, nor was it seen in all three limb leads. Stewart and Manning found two examples of notching in these three leads, but they did not specify its degree. The incidence of notching in the limb leads I and II, low though it is, is probably too high to regard the sign as unequivocal evidence of myocardial damage unless it is associated with a similar change in the chest leads.

TABLE I

THE INCIDENCE AND DEGREE OF NOTCHING OF THE QRS COMPLEX IN SEPARATE OR COMBINED LEADS IN 156 HEALTHY SUBJECTS

	Leads	I	II	III	I and II	I and III	II and III	I, II, and III
Degree	Slight	2	—	25	—	1	4	1
	Moderate	1	—	14	—	—	3	1
	Prominent	—	—	17	—	—	1	—
	Total	3	None	56	None	1	8	2
	Leads	CR1	CR4	CR7	I and CR1	III and CR1	II, III, and CR1	I, III, and CR4
Degree	Slight	10	1	1	1	21	2	1
	Moderate	2	—	—	—	4	—	—
	Prominent	1	—	—	—	4	2	—
	Total	13	1	1	1	29	4	1

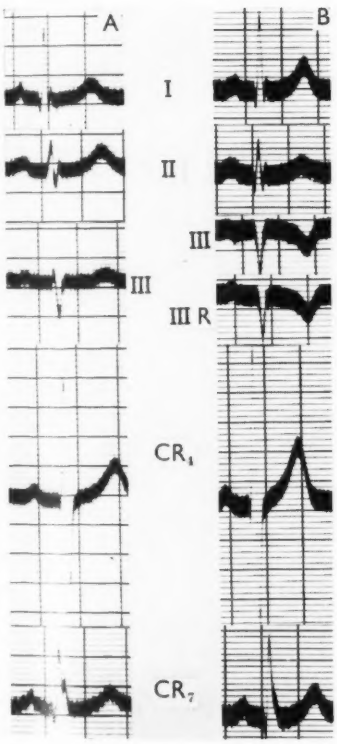

FIG. 2.—Notching of the QRS in cardiac pain. Prominent notching in CR7 is a lone sign in (A), taken three years before (B), which shows added signs of infarction in the form of a deep Q and an inverted T wave in leads III and III R.

It was common to find notching in CR1 (45 out of 156) and approximately the same incidence was found for CR2 and CR3, and the change was often present in two or all three leads. We know that notching in these leads can be a pathological sign because we have seen it develop along with other graphic evidence of cardiac infarction and persist as the only sign when the cardiogram had otherwise resumed a normal pattern. It is true that such notching was on the ascending limb of the R wave, but this does not wholly differentiate the pathological from the physiological curve, and in the meantime it cannot be regarded as having diagnostic value. Notching of the QRS in CR4 was only found once in our healthy series when it was very slight and associated with similar notching in leads I and III; in this instance there was also notching in CR3 and CR5. With this exception and recently in a healthy youth of 22, not included in our series, who showed slight notching in CR7, the change was not found in leads CR4 to CR7. There is agreement that notching can take place over the so-called transition zone (Wilson *et al.*, 1944; Rosenman and Reynolds, 1950) which varies in position and width. Our case of notching in CR4 and CR5 occurred when both leads showed an Rs complex.

On the other hand, among patients with chest pain, we have found several examples of notching of CR7 and less frequently of CR4 when this lead showed a qR pattern. The notching is usually on the downstroke of the R wave and it is often associated with similar notching in a limb lead. Such a change may be a lone cardiographic finding or appear alongside other slight abnormalities like S–T depression. We regard the sign as indicating myocardial damage, and cardiac infarction in a patient with chest pain (Fig. 2). We have also found this sign in patients showing left ventricular preponderance from hypertension, most of whom had cardiac pain; even in cases of hypertension without pain we regard the sign as pointing to coronary arterial disease.

Depression of the S–T Segment

A deformity of the S–T interval showing as a depression is a common finding in early myocardial injury from coronary artery disease. Such depression may not extend obviously below the isoelectric level and usually only part of the segment is involved. Thus, the change may happen in the early, middle, or distal portions of the S–T interval and much or even the whole of the segment may not fall below the baseline (Fig. 3).

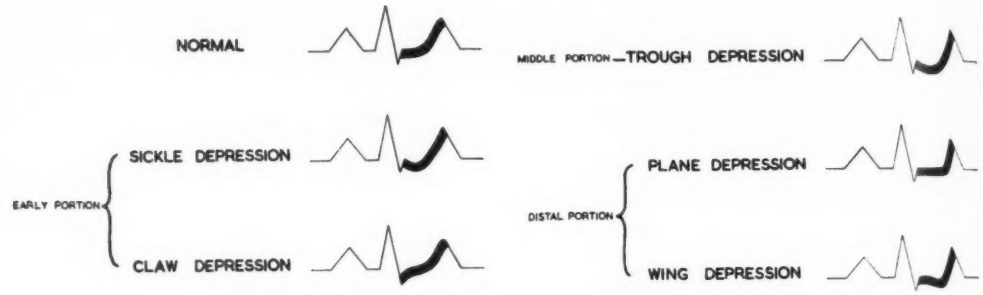

FIG. 3.—Diagram showing the different forms of S–T depression in cardiac pain.

Depression of the early portion of the S–T. Such depression was not met with in the healthy series, but was sometimes seen in patients with chest pain whose electrocardiograms at one time were regarded as normal or only showing equivocal changes, but where cardiac infarction was ultimately proved to be the cause of the pain. The deformity in this group was of two kinds. The first was a small dip after the start of the segment resulting in a *sickle depression* (Fig. 4). This was made more obvious when an R1 wave immediately preceded it. In the second kind the depression is earlier and affecting the returning limb of the S wave producing a *claw depression.* Like the first variety this is not a common deformity. It may be difficult of interpretation and it should not be confused with a broad S wave which always forms an angle at the point where it joins the S–T segment (Fig. 5). In the pathological claw depression on the other hand, the S–T is depressed below the isoelectric level from its very commencement at the peak of the S whence it passes upwards as an upward convex curve to reach the isoelectric line (Fig. 6).

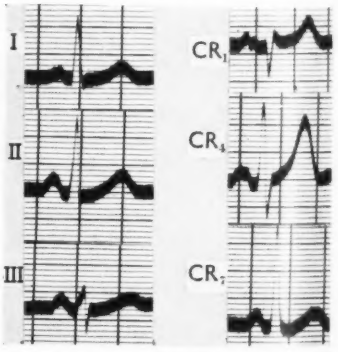

FIG. 4.—Sickle depression of S–T in cardiac pain. This deformity in CR7 is the only abnormal sign in the resting cardiogram. The exercise test gave a positive result.

Depression of the middle portion of the S–T. This deformity too was not found in the healthy series, but appeared in those patients with cardiac pain and minor cardiographic changes. The resulting curve which is in the form of a *trough depression* (Fig. 7) is again seen to better advantage when an R1 precedes it.

Depression of the distal portion of the S–T. This deformity is noteworthy in that the segment may not at any point reach below the isoelectric line. It deserves the term depression, however, because the terminal portion is depressed compared with the corresponding portion of the normal segment. As a result, the segment is linear as far as the more acute angle that it forms with the ascending limb of the T wave; this limb is unusually steep because its formation is delayed. We have named this deformity the *plane depression* and we regard it as the most valuable of the lesser cardiographic signs of cardiac pain (Fig. 8 and 9). Sometimes the whole segment may be displaced

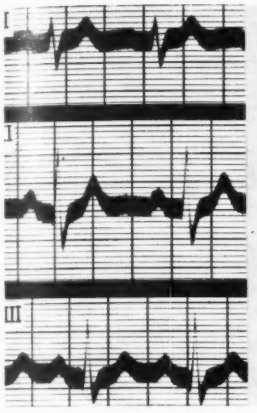

FIG. 5.—Broad S wave in health simulating claw depression of S–T. The returning limb of the S wave is wide but is not depressed.

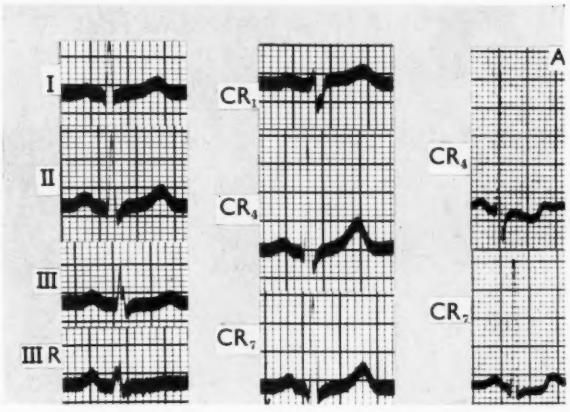

FIG. 6.—Claw depression of the S–T in cardiac pain. This deformity in leads II, III, and CR7, along with lowering of the T in III R, are the only abnormal signs in the resting cardiogram. The exercise test gave a positive result (A).

downwards while retaining this characteristic flattening, when its significance is the same and the difference is one of degree only.

An exaggerated form of this depression is met with where the end of the S–T interval dips below the isoelectric level, making with the ascending limb of the T wave a curve resembling the lapwing in flight, and for this reason we have referred to it as *wing depression*. In patients with cardiac pain this deformity was less common than the plane variety when the cardiogram was recorded at rest, but it was common as part of the abnormal curve that followed cardiac anoxæmia induced by physical exercise (Fig. 10).

S–T depression in III R. A comparison of the S–T segment in lead III with that seen in III R (lead III during deep inspiration) proved valuable in the detection of lesser ischæmic changes. A code of normality has been nominated for III R (Evans, 1951) and this concerns the Q and T waves in addition to the S–T segment. A depression of the S–T does not appear in health except in the rare instances when the heart moves upwards during inspiration (paradoxical movement of the diaphragm) (Fig. 11), and sometimes when the heart hangs vertically in the chest. This depression of the S–T in III R may affect any part of the segment and it was found either in company with other minor cardiographic effects of cardiac ischæmia or as a lone sign (Fig. 12 and 13). The presence of the sign depends on the site of the infarct, so that it was present when the injury was situated in the lateral, posterolateral, and postero-inferior parts of the left ventricle, and occasionally in the septum, but not when the infarct was placed anteriorly. The usefulness of III R, therefore, depends on its sensitiveness to changes in three out of the five areas in the heart that are commonly affected by infarction.

THE R1 WAVE

By definition the R1 wave is the upright wave immediately following the S wave, but the designation is not used here to describe the large secondary R wave found in leads over the right ventricle in patients with right bundle branch block. When studying the less obvious cardiographic changes in patients with chest pain we found the R1 wave in many of them; it was present either in company with other minor though significant changes or was the only obvious change. We next looked for it in the healthy series of 156 cases and found it in 45 of them (Fig. 14). The particular leads that showed R are listed in Table II, and when the incidence of R1 in single or combined leads was compared

with that found in cases with chest pain the two groups could not be distinguished. It caused some surprise that the presence of R1 should prove to be less significant than prominent notching of the QRS complex, but the analysis of the two series of cases does not justify the conclusion that the presence of the wave by itself signifies myocardial injury.

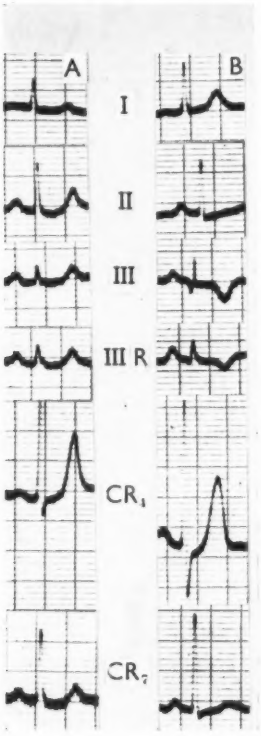

FIG. 7.—Trough depression of the S–T in cardiac pain. This deformity in leads II, III, III R, and CR7 in (A) is replaced by more obvious signs of cardiac infarction in (B), recorded 15 months later.

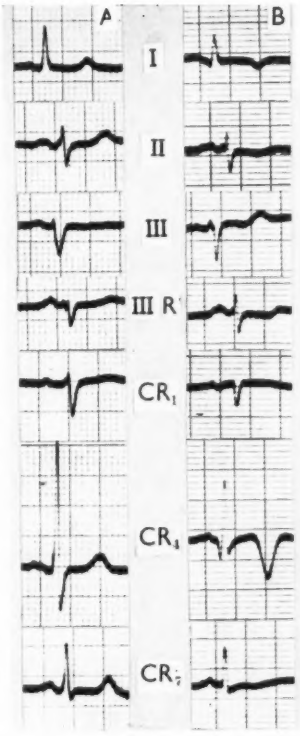

FIG. 8.—Plane depression of the S–T in cardiac pain. This deformity in leads I and CR7 with a low T in CR4 (A), gave way to more obvious changes three years later (B).

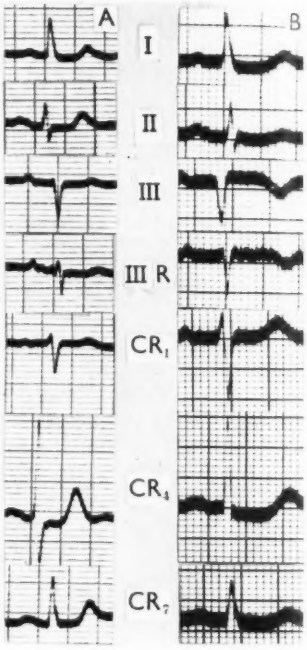

FIG. 9.—Plane depression of the S–T in cardiac pain. This deformity in leads I, II, CR4, and CR7 (A) was followed eight months later by more obvious signs of infarction (B).

CHANGES IN T WAVES

The low T wave. It is known that the height of the T wave varies among healthy subjects and from lead to lead. This variation applies not only to its absolute amplitude, but also in its relationship to the height of the R wave. One would expect that between the normal upright and the abnormal flat T wave there should be an intermediate stage where a lowered T could be regarded as an abnormal sign. The difficulty lies in the definition of the lower limits of normal. Dressler (1943) tried to overcome this by comparing the amplitude of T waves in different leads, but Goldberger (1947) has disputed the accuracy of this procedure in the case of limb leads. Leatham (1950) calculated the height of the T wave in chest leads and its relation to the height of the R wave: in

TABLE II

INCIDENCE OF R1 WAVE IN THE LIMB AND THREE CHEST LEADS OF 156 HEALTHY SUBJECTS

Leads	I	II	III	I and II	I and III	II and III	I, II, and III	
Incidence	2	6	7	—	—	6	—	
Leads	CR1	CR4	CR7	I and CR7	II and CR7	III and CR7	CR4 and CR7	I, II, and CR7
Incidence	6	5	2	2	2	1	1	1

CR4 the average height of the T was 7·9 mm. and this was 26 per cent of the average amplitude of the R wave. The corresponding figures for CR7 were 3·3 mm. and 29 per cent. We obtained similar figures in a further series of healthy subjects, but the variation proved so wide as to make such measurements of little value.

Although a low T wave is met with in CR4 in health its presence in a patient with chest pain should always be regarded with suspicion and another tracing should be recorded after exercise. Should the low T wave be a pathological sign in the cardiogram at rest, exercise should produce a positive test (Fig. 8, 15, and 16). On the other hand a negative test is expected if the low T is part of a physiological cardiogram. A low T wave is unusual in CR7 in health and for this reason it is a valuable sign; this does not apply to V7 where the normal T is expected to be low. A low T in lead I may occur in health, but when it is associated with a low T in CR4 and especially in CR7 it is likely to be significant.

The blunt T wave. A blunted T wave, where the customary sharp peak is pruned giving it a domed appearance, is not necessarily a low T wave for the change is confined to the summit of the

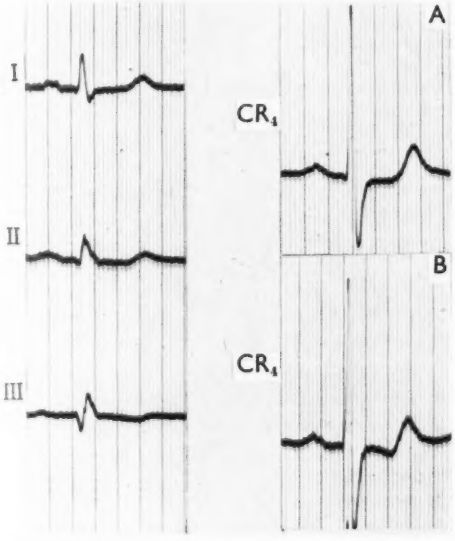

FIG. 10.—Wing depression of S–T in cardiac pain. A plane depression in the resting CR4 cardiogram (A) changed to wing depression after exercise (B).

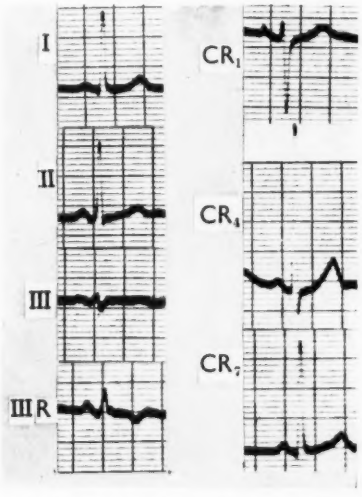

FIG. 11.—Paradoxical movement of diaphragm. In a case where left phrenic nerve had been divided in the treatment of tuberculosis, inspiration caused the left dome of diaphragm to move upwards and inversion of the T wave in III R.

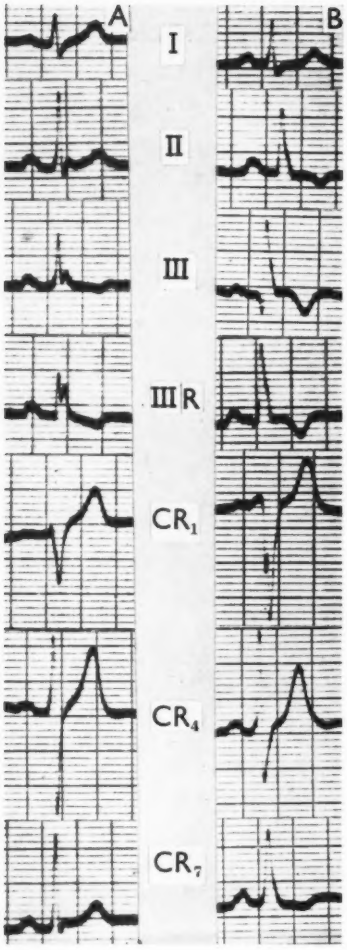

FIG. 12.—Depression of S–T in III R in cardiac pain. This deformity is a lone sign in (A) recorded two months before the more obvious signs of cardiac infarction appeared (B). Patient died during an attack of pain six months later.

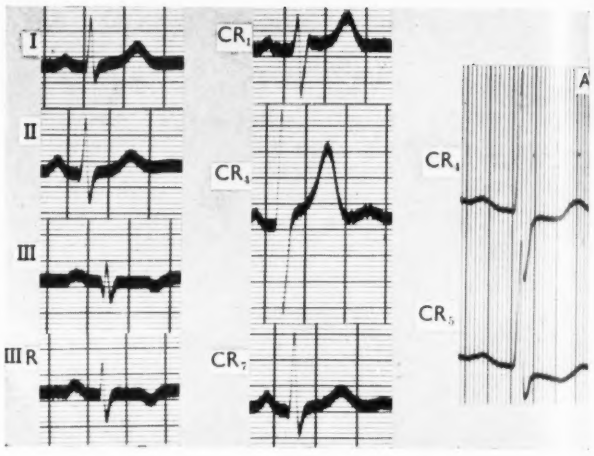

FIG. 13.—Depression of S–T in III R in cardiac pain. A lowering of terminal portion of S–T and further inversion of T are the only abnormal signs in the resting cardiogram. A positive exercise test was obtained (A).

wave, although for that reason the wave naturally loses a little of its stature. Indeed, this slight lowering distinguishes it from a blunted tall T wave which is occasionally met with in health. From their study of the allied deformity of notching of the T wave, Dressler *et al.* (1951) concluded that such a deformity had the same significance as T wave inversion; and that slurred, flat-topped, and triphasic T waves were closely related to notched T waves and had the same meaning. A blunted and slightly depressed T wave in CR4 or CR7 was not met with in our healthy series, and although it was not a frequent finding in those cases with chest pain and equivocal cardiographic changes, its presence even as a lone finding told of a myocardial injury (Fig. 17 and 18) and for that reason we regard it as an important sign.

Terminal dipping of the T wave. We have been hesitant about including this change among the less obvious cardiographic signs, because its recognition is not difficult as a rule when it gives to the T wave a diphasic conformation. It is when this deformity is minimal in a tracing taken either early in the illness of cardiac infarction or during recovery that it may assume importance in that it

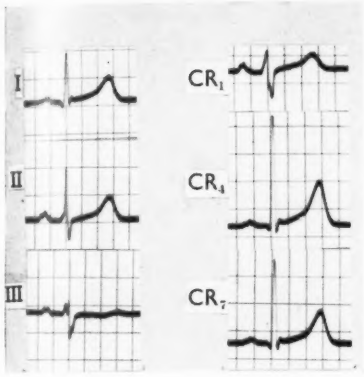

FIG. 14.—The R1 wave in health. This small upright wave immediately follows the S wave in leads I, CR4, and CR7.

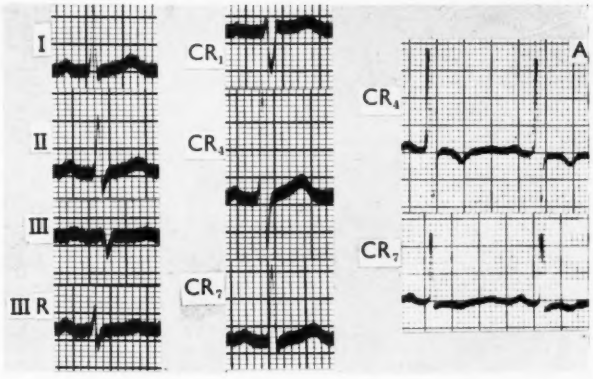

FIG. 15.—Low T wave in cardiac pain. A low T in CR4 is the only suspicious sign in the resting cardiogram; it became inverted after exercise (A).

may then go undetected (Fig. 19 and 20). Care should be taken not to mistake as terminal dipping of the T an appearance where through tachycardia an early incidence of the P wave may prevent the completion of the descending limb of the U wave so that the natural dip between the T and U waves is no longer matched by a similar bay between the U and P waves (Fig. 21).

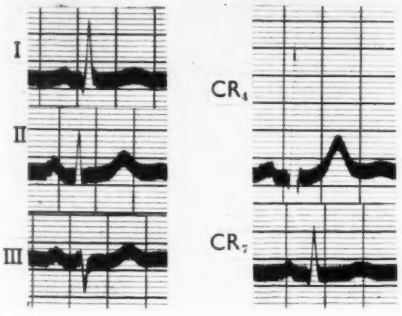

FIG. 16.—Low T wave in cardiac pain. A low T in leads I and CR7 is the only noticeable change in the tracing from a patient who died suddenly three months later from an extension of cardiac infarction.

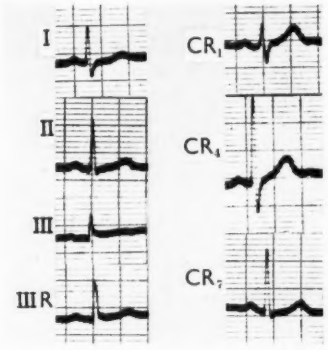

FIG. 17.—Blunt T wave in cardiac pain. This deformity in lead CR4 is the main cardiographic change in a patient who died six months later from further cardiac infarction.

INVERSION OF THE U WAVE

The sixth wave has attracted attention since the early days of electrocardiography and Einthoven (1906) at first thought it was abnormal, but later he realized that it could be found in health (Einthoven, 1912). Others (Lewis and Gilder, 1912) have described a peaked variety of short duration and a long shallow kind, and Maekawa (1931) considered that the second variety was pathological. There is general agreement now that an upright U wave is a normal finding irrespective of contour, but such unanimity of opinion is not found concerning inversion of the U wave. Katz (1946)

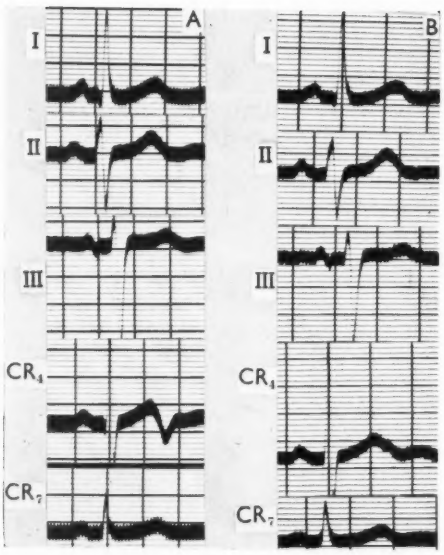

FIG. 18.—Blunt T wave in cardiac pain. This deformity of T in CR4 in (B) is the only residual sign of cardiac infarction nine months before (A).

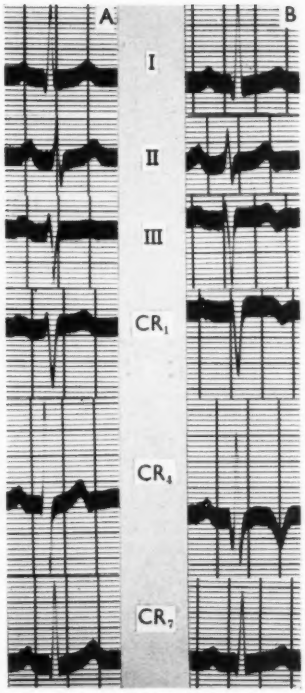

FIG. 19.—Terminal dipping of T wave in cardiac pain. This change in CR4 (A) preceded by four months the more obvious signs of cardiac infarction shown in (B).

stated that little clinical weight should be allocated to a cardiogram in which the only deviation from the normal was in the U wave, and Solarz and Elek (1943) said that a study of U wave patterns was of little value in diagnosis. Others, however, have been at variance with these views. Thus, Nahum and Hoff (1939) found an inverted U wave only when heart disease was present and at times it was the only cardiographic evidence of myocardial damage, while Palmer (1948) concluded that inversion of U in one or more leads should always be regarded as pathological.

Inversion of the U wave was not met with once in our healthy series. Other workers have had identical experience, among them Stewart and Manning (1944) using limb leads only, and Myers *et al.* (1947) using a full range of chest leads in a smaller series. Graybiel *et al.* (1944) using limb, CR4, and CF4 leads in 1000 cases found inversion of U twice, and in both the change was confined to lead III; they did not state whether the change was associated with inversion of the T wave as well, nor did they test the effects of deep inspiration on the inversion. The infrequency with which inversion of the U wave has been reported in healthy subjects and its presence with other cardiographic changes in patients with heart disease (Nahum and Hoff, 1939; Papp, 1940; Solarz and Elek, 1947; Palmer, 1948) makes it very likely that the finding is pathological. Although it has usually been found in coronary artery disease, it has also been reported in hypertensive, valvular, and pulmonary heart disease. Palmer found inversion of the U wave in two cases of hypertension where coronary artery disease appeared to be absent. We found it three times in patients with

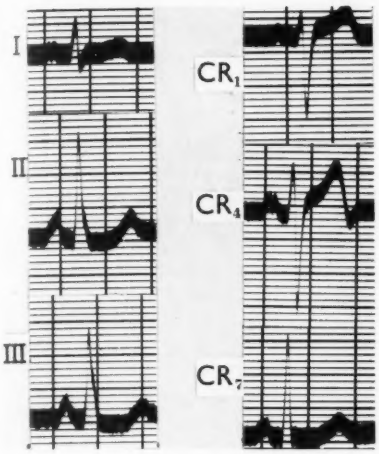

FIG. 20.—Terminal dipping of T wave in cardiac pain. This deformity in CR4 is the most noticeable change in a patient who later showed more obvious signs of cardiac infarction.

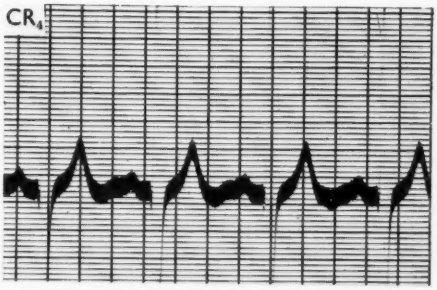

FIG. 21.—Apparent dipping of T wave caused by tachycardia. Early incidence of the P wave has interrupted the descending limb of the U wave giving a false impression of terminal dipping of the T.

left ventricular preponderance from hypertension in whom cardiac pain was absent, and we have found it once in patent ductus arteriosus where the cardiogram showed early left ventricular preponderance. Our experience leads us to emphasize caution in the diagnosis of an inverted U wave where the dip is not obvious, but we believe that true inversion of the U wave, either in the first two limb leads or in CR4 in the absence of other heart disease, is evidence of myocardial damage from coronary atheroma; proof of this will evolve from the natural progress of the case or from the test of cardiac anoxæmia (Fig. 22 and 23).

SUMMARY AND CONCLUSIONS

Experience has shown how unreliable is the patient's description of his pain as a guide to the diagnosis of coronary artery disease. It is known too that physical signs are sparse, and the electrocardiogram alone can provide the information that may save a patient from unwarranted invalidism created by a faulty interpretation of the chest pain in the absence of this test.

It was for this reason that we undertook an investigation of the lesser cardiographic signs found in cardiac-like pain, which hitherto have not been acknowledged as evidence of coronary artery disease. We first sought these changes in tracings from 156 healthy subjects and afterwards in those from patients where myocardial damage had been confirmed. Before accepting a particular cardiographic sign as proof of such heart disease we required, in addition to its absence from the healthy series, that the tracing in patients with cardiac pain should demonstrate undisputed cardiac infarction on another occasion, or that a one-time physiological cardiogram, recorded fortuitously when cardiac pain was absent, should subsequently show the lesser changes following the onset of pain; or that the less obvious changes should be joined by those typifying increased cardiac ischæmia in the course of the exercise test; or that cardiac infarction should have been discovered at necropsy in a patient who had only shown the less obvious signs at a recent cardiographic examination.

The investigation has allotted to these lesser changes in the electrocardiogram a significance no less important than the presence of Q waves and/or inverted T waves. Actually, the mortality rate,

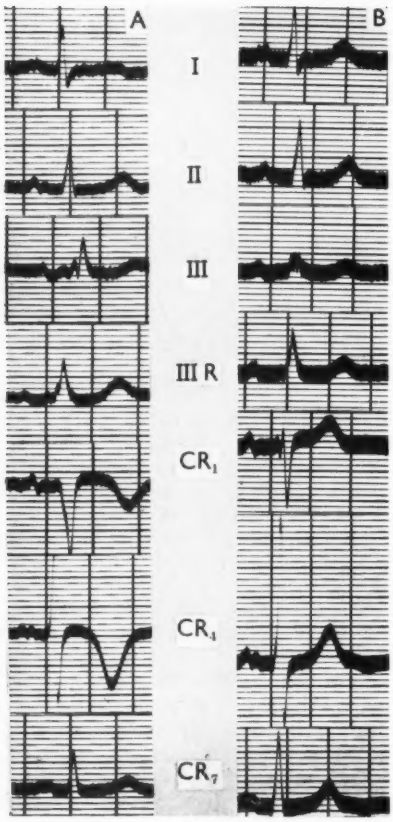

FIG. 22.—The U wave in cardiac pain. Inversion of U in CR4 (B) is the only residual sign of cardiac infarction three years before (A).

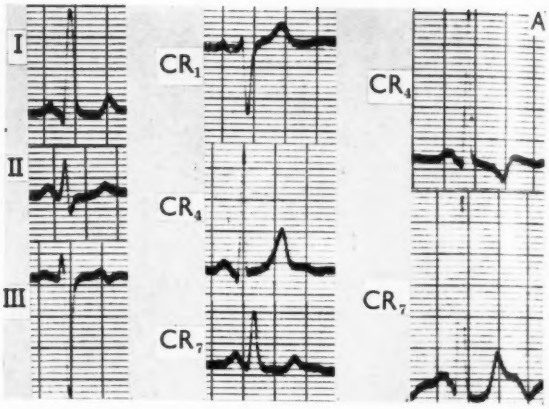

FIG. 23.—The U wave in cardiac pain. Plane depression of S–T in I and CR7 and inversion of U in CR4 are the only changes in the resting cardiogram. After exercise (A) the T as well as the U is inverted in CR4, and U wave inversion becomes a conspicuous change in CR7.

for patients showing the more obvious changes is no greater than for those showing the lesser changes, and since both types of cardiogram indicate myocardial damage from coronary artery disease, they hold equal place in its diagnosis and prognosis.

A wave in the P–Q period or an R1 wave sometimes preceded or appeared alongside the characteristic changes of cardiac infarction; their frequent occurrence in health, however, excluded them as specific signs of myocardial injury. The lesser cardiographic changes that did signify such injury from coronary artery disease included notching of the QRS complex, depression of the S–T segment, a low or blunt T wave, dipping of the terminal limb of the T wave, and an inverted U wave.

Slight notching of the QRS, particularly in lead III and in chest leads over the right ventricle, is common in health. Moderate or greater notching in chest leads over the left ventricle which show a qR pattern is evidence of a myocardial injury.

Depression of the S–T segment was a common change in patients with cardiac pain and it proved to be the most significant of the lesser cardiographic signs. Frequently, such depression involved only a portion of the S–T segment and did not over-reach the isoelectric level. Depression of its early portion produced either a *claw* or a *sickle* deformity and was less common than a *trough* depression involving the middle portion of the S–T segment; this deformity was a particular feature of lead III R (lead III during deep inspiration). Depression of the distal portion of the S–T segment produced either a *plane* or a *wing* deformity. Plane depression of the S–T segment proved

to be a common sign and we apportion to it exceptional value in the diagnosis of cardiac pain. Wing depression was a less common abnormal finding in the resting cardiogram, but it frequently appeared as part of the deformity characterizing the positive exercise test.

Although a low T wave may be found in lead I and/or in CR4 in healthy subjects, it should be viewed with suspicion in a patient with chest pain, and another cardiogram recorded following exercise. A low T wave in CR7 is seldom met with in health and when the deformity signifies myocardial injury it is accompanied by a low T in lead I and depression of the S–T segment in III R.

A blunted T wave in CR4 or CR7 with a slight loss of height is a pathological change, as also is dipping of its terminal limb below the isoelectric level.

Inversion of the U wave appearing in the first two limb leads and especially in CR4, in the absence of other heart disease, is evidence of myocardial injury from coronary artery disease.

The recognition of these lesser cardiographic signs contributes to a readier diagnosis of cardiac pain and reduces significantly the number of such patients regarded in the meantime as having a normal electrocardiogram.

Of those patients attending the Cardiac Department, some were under the care of Dr. Wallace Brigden. Many of the electrocardiograms in healthy subjects were recorded by Dr. Aubrey Leatham when he was Sherbrook Research Fellow, and Dr. Geoffrey Storey helped with the exercise tests when he was Registrar to the Department.

References

Bayley, R. H. (1946). *Amer. Heart J.*, **31**, 677.
Carter, E. P. (1914). *Arch. intern. Med.*, **13**, 803.
—— (1918). *Arch. intern. Med.*, **22**, 331.
Dressler, W. (1943). *Amer. Heart J.*, **26**, 313.
——, Roesler, H., and Lackner, H. (1951). *Brit. Heart J.*, **13**, 496.
Einthoven, W. (1906). *Arch. Internat. Physiol.*, **4**, 132.
——, (1912). *Lancet*, **1**, 853.
Evans, W. (1951). *Brit. Heart J.*, **13**, 457.
Goldberger, E. (1947). *Amer. Heart J.*, **34**, 395.
Graybiel, A., McFarland, R. A., Gates, D. C., and Webster, F. A. (1944). *Amer. Heart J.*, **27**, 524.
Hall, G. E., Stewart, C. B., and Manning, G. W. (1942). *Can. med. Assoc. J.*, **46**, 226.
Herrick, J. B. (1919). *J. Amer. med. Assoc.*, **72**, 387.
Katz, L. N. (1946). *Electrocardiography*. 2nd ed., Kimpton, Lond.
Leatham, A. (1950). *Brit. Heart J.*, **12**, 213.
Lewis, T., and Gilder, M. D. D. (1912). *Phil. Trans. Roy. Soc.*, **202**, 351.
Maekawa, M. (1931). *Acta. Sch. Med. Univ. Kioto*, **14**, 16.
Master, A. M., Friedman, R., and Dack, S. (1942). *Amer. Heart J.*, **24**, 777.
Myers, G. B., Klein, H. A., Stofer, B. E., and Hiratzka, T. (1947). *Amer. Heart J.*, **34**, 785.
Nahum, L. H., and Hoff, H. E. (1939). *Amer. Heart J.*, **17**, 585.
New York Heart Association. *Crit. Com.* (1940). New York.
Palmer, J. H. (1948). *Brit. Heart J.*, **10**, 247.
Papp, C. (1940). *Brit. Heart J.*, **2**, 9.
Pardee, H. E. B. (1920). *Arch. intern. Med.*, **26**, 244.
Parkinson, J., and Bedford, D. E. (1928). *Heart.*, **14**, 195.
Rosenman, R. H., and Reynolds, R. W. (1950). *Amer. Heart J.*, **40**, 867.
Solarz, S. D., and Elek, S. R. (1943). *J. Lab. Clin. Med.*, **28**, 936.
Stewart, C. D., and Manning, G. W. (1944). *Amer. Heart J.*, **27**, 502.
Wedd, A. M., (1919). *Arch. intern. Med.*, **23**, 515.
Weinberg, S. L., Reynolds, R. W., Rosenman, R. H., and Katz, L. N. (1950). *Amer. Heart J.*, **40**, 745.
Wilson, F. N., and Hermann, G. R. (1920). *Arch. intern. Med.*, **26**, 153.
——, Johnston, F. D., Rosenbaum, F. F., Erlanger, H., Kossmann, C. E., Hecht, H., Cotrim, M., De Oliveira, R. M., Scarzi, R., and Barker, P. S. (1944). *Amer. Heart J.*, **27**, 19.
Wolferth, C. C., and Wood, F. C. (1932). *Amer. J. med. Sci.*, **183**, 30.
Wood, P., McGregor, M., Madgison, D., and Whittaker, W. (1950). *Brit. Heart J.*, **12**, 363.

CARDIOGRAPHIC STUDIES IN SEVERE PULMONARY EMPHYSEMA

BY

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The introduction of cardiac catheterization has offered the possibility of a further aid to the early diagnosis of emphysema heart disease by direct measurement of right ventricular pressures. In this paper cardiographic findings have been related to right ventricular pressures in severe pulmonary emphysema. Similar studies have been carried out by Johnson *et al.* (1950) and Kilpatrick (1951).

Material and Methods

All of the sixteen cases were diagnosed clinically as chronic bronchitis and emphysema, and suspected of having heart disease secondary to their emphysema. In every case respiratory studies were carried out confirming the presence of severe emphysema. Eight of the patients had systemic hypertension in addition to chronic bronchitis and emphysema but none was considered to have evidence of left ventricular failure.

Clinically, the patients fell into three main groups at the time of cardiac catheterization: those who had never been in heart failure, those in congestive failure, and those recovering from congestive failure. Congestive failure was considered to be present when the jugular venous pressure was found to be raised, whether or not œdema was present. Unless œdema had developed, it was difficult to fix the time of onset of cardiac failure adequately from the clinical history, since symptoms due to emphysema heart disease were gradually superimposed upon those of pulmonary emphysema.

Measurements of right ventricular pressure were recorded by strain gauge manometry, as described previously by Bayliss *et al.* (1950).

Cardiographic exploration included standard leads, augmented unipolar limb leads, and at least four chest leads V5, V3, V1 and V4R. The technique used did not permit measurement of time intervals on the tracings more closely than to an hundredth of a second.

The cardiograms were recorded as far as possible within a few days of the date of catheterization. In eight cases, however, a longer interval separated the two investigations. This interval was a week in five cases and between two to three weeks in three. It was not considered that this invalidated the correlation of right ventricular pressures with the cardiogram in these cases, since in those patients in whom more frequent serial cardiograms were taken no significant cardiographic changes were noticed over a similar period of time, even under the stress of an episode of congestive cardiac failure.

The cardiographic criteria for the diagnosis of right ventricular hypertrophy were based on the findings of Wilson *et al.* (1947), later amplified by Myers *et al.* (1948). Myers described three patterns in right ventricular hypertrophy. The first pattern, which he considered diagnostic of right ventricular hypertrophy, showed (1) a prolonged time interval between the beginning of the QRS complex and the onset of the intrinsicoid deflection in V1, generally between 0·03–0·05 second,

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which was greater than that in V5 and V6; (2) a total duration of the QRS complex less than 0·12 second; (3) a tendency to a small Q wave in V1; (4) a reversal of the ratio of amplitudes of the R and S waves in V1 and V6, characterized by an abnormally large R in proportion to S in V1, and a prominent S in V6; (5) a tendency to inversion of T in V1 and to an upright T in V6; and (6) absence of notching of R in V1 except where preceded by a Q wave. In the second pattern of Myers the cardiographic picture just described in lead V1 was confined to V3R and was not seen in V1. Myers' third pattern, in which lead aVR alone gave evidence of right ventricular hypertrophy, was not met in our series. We have used leads V5 and V4R routinely instead of V6 and V3R respectively.

An RSR′ pattern was met in our series in which (1) the total duration of the QRS complex did not exceed 0·12 second; (2) the time interval from the beginning of the QRS complex to the peak of the final R wave in V1 was between 0·05–0·07 second; (3) Q waves were absent from leads on the right side of the præcordium; and (4) notched or double-peaked R waves were present in leads from the right side of the præcordium, while in leads from the left side there tended to be prominent S waves.

The diagnosis of complete right bundle branch block was made when (1) the total duration of the QRS complex was 0·12 second or longer; (2) the peak of the final R wave in lead V1 was later in time than the peak of the R wave in V5; and (3) in leads from the right side of the præcordium R waves were prominent, coarsely notched, or double-peaked, and Q waves were absent.

Results

There were thirteen men and three women in the series, the average age being 50·9 years. In all cases the residual air expressed as a percentage of total lung volume was greatly raised, the average value being 67 per cent (normal range 16 to 40 per cent). Half of the patients had systemic hypertension in addition to pulmonary emphysema, our upper limits of normal systemic blood pressure being 150 systolic and 90 mm. Hg diastolic.

Right Ventricular Pressures. On cardiac catheterization, in the absence of congestive failure, the right ventricular systolic pressure was found to be normal or only moderately raised. In the presence of failure, however, pressures were significantly raised in every case. As patients recovered from failure, restoration of their right ventricular pressures towards normal occurred. The pulmonary hypertension seen in heart failure in emphysema therefore was reversible, a finding in agreement with previous studies by Borden *et al.* (1950), Ferrer *et al.* (1950), and Harvey *et al.* (1951). Details of right ventricular pressure records are given in Table I, where it will be seen that eleven cases had raised resting systolic pressures in the absence of heart failure, the upper limit of normal being taken as 30 mm. Hg.

Cardiograms. On analysis of the cardiograms the cardiographic picture of right ventricular hypertrophy was found in two of the sixteen cases. Nine patients showed no cardiographic evidence of right ventricular hypertrophy, and one had complete right bundle branch block. Four showed an RSR′ pattern in right præcordial leads, which was persistent on serial graphs over a period of at least six weeks.

In five cases in whom two sets of right ventricular pressures were measured, both in failure and on recovery from failure, the analysis of only one cardiogram is shown for each patient, since no significant differences were noted in corresponding serial cardiograms.

Effect of Associated Systemic Hypertension on the Cardiogram. Associated systemic hypertension appeared to modify the cardiographic pattern in left chest leads. In the series as a whole small R and large S waves were usually seen in these leads, irrespective of the presence or absence of evidence of right ventricular hypertrophy in right chest leads. It was thought that this was due to the vertical position of the heart in emphysema. In the eight cases where there was associated systemic hypertension, a larger R and smaller S wave was seen in left chest leads, but in no case was the cardiographic picture of left ventricular hypertrophy present.

TABLE I

Clinical and Physiological Findings								Cardiographic Findings						
Case No.	Age	Sex	Residual air × 100 ÷ Total lung volume	Systemic Blood Pressure (mm. Hg)	Resting Right Ventricular Pressures			V4R		V1		V5		Cardiographic diagnosis
					Not in failure (mm. Hg)	In failure (mm. Hg)	Recovering from failure (mm. Hg)	Onset of QRS to peak of R wave (sec.)	R/S Ratio	Onset of QRS to peak of R wave	R/S Ratio	Onset of QRS to peak of R wave	R/S Ratio	
20	40	M	68	135/75		43/8	19/−5			0·01	0·1	0·02	0·9	No evidence of right ventricular hypertrophy
1	52	M	82	160/80	17/1			0·01	0·1	0·01	0·1	0·02	2	
6	40	M	80	145/90	42/3			0·02	0·2	0·02	0·3	0·02	0·3	
5	62	M	63	170/90	34/5			0·02	0·5	0·02	0·5	0·05	17	
16	44	M	58	130/80			41/4			0·02	0·1	0·03	1·2	
2	68	M	71	145/90	26/5			—	—	—	—	0·03	1·7	
17	54	M	62	130/90			30/−1	0·02	0·1	0·02	0·1	0·03	0·6	
21	60	M	56	200/105		63/14	20/0	0·01	0·1	0·02	0·3	0·03	10	
8	52	F	57	170/100	53/5					0·01	0·4	0·04	4	
23	51	F	56	140/100		71/11	51/4	0·06	3	0·06	3	0·01	2	Right ventricular hypertrophy
24	45	M	76	130/90		83/18	46/4	0·05	1·5	0·05	2	0·02	0·1	
								Onset of QRS to peak of R′ wave (sec.)	R′/S Ratio	Onset of QRS to peak of R′ wave (sec.)	R′/S Ratio			
4	52	M	74	130/80	31/−1			0·05	0·1	—	—	0·02	3	RSR′ pattern
19	60	F	69	175/115			49/−3	0·05	1	—	—	0·04	6	
22	46	M	70	140/100		71/9	43/0	0·05	4	0·05	1·6	0·03	1·7	
7	62	M	62	115/60	46/2			0·06	2	0·05	0·6	0·04	0·5	
18	27	M	66	130/110			42/6	0·08	4	0·08	4·5	0·04	4	Complete R.B.B.Bl.

Case numbers are identical with those used in previous hæmodynamic study of the same cases (Mounsey *et al.* (1952). *Brit. Heart J.*, **14**, 153).

Autopsy findings. Autopsy confirmation of emphysema heart disease was obtained in Case 16. A grossly hypertrophied right ventricle was found, the anterior wall of the outflow tract at a point 2 cm. below the pulmonary valves, measuring 10 mm. in thickness. The lungs showed evidence of chronic bronchitis and vesicular emphysema. The cardiogram is illustrated in Fig. 1, the first

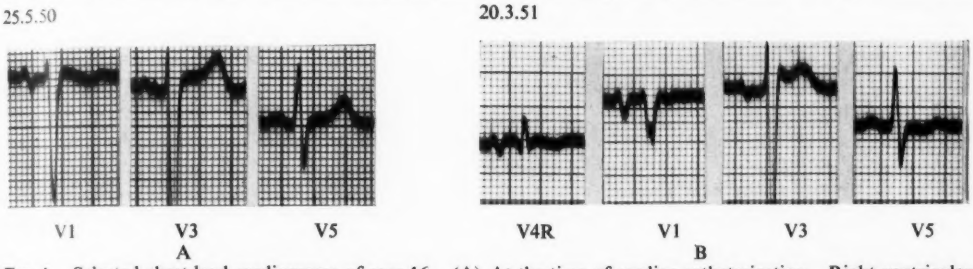

FIG. 1.—Selected chest lead cardiograms of case 16. (A) At the time of cardiac catheterization. Right ventricular pressure raised (41/4 mm. Hg). No cardiographic evidence of right ventricular hypertrophy. (B) Two months before death. At autopsy gross right ventricular hypertrophy. Cardiogram shows QR pattern of right ventricular hypertrophy in V4R.

tracing (A) being at the time of cardiac catheterization, when cardiographic evidence of right ventricular hypertrophy was absent. The second tracing (B) was taken two months before death and shows evidence of right ventricular hypertrophy confined to lead V4R.

THE EMBRYONIC R WAVE, THE RSR′ PATTERN, AND RIGHT VENTRICULAR HYPERTROPHY

In Fig. 2, the QRS patterns found in leads V1 and V4R of the sixteen patients at the time of catheterization are illustrated diagrammatically. They have been divided into eight different patterns. It will be seen that there is an apparent progression in the height of the secondary R

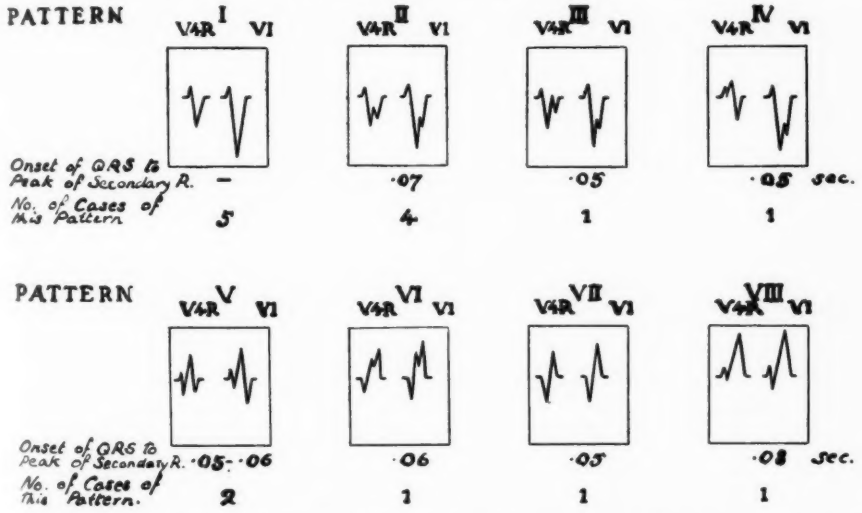

FIG. 2.—Diagram illustrating QRS patterns in V1 and V4R seen in sixteen cases of severe pulmonary emphysema. There appears to be a progressive increase in size of the secondary R wave in patterns II to VII, starting with an embryonic R wave in pattern II and ending with the secondary R wave of the RSR′ pattern in patterns III, IV and V and with the final R wave of right ventricular hypertrophy in patterns VI and VII. Pattern VIII shows complete right bundle branch block.

wave, starting from a small embryonic R wave * in pattern II and ending with a secondary R wave in patterns III, IV, and V (RSR′ complex) and with a final R wave in patterns VI and VII (right ventricular hypertrophy). Pattern VIII is an example of complete right bundle branch block. The timing of the embryonic R waves lay between 0·05–0·07 second after the beginning of the QRS complex.

In an effort to determine the significance of embryonic R waves in lead V1 and V4R, cardiograms were recorded in a series of 30 healthy men, aged between 20 and 40. An embryonic R wave in V1 and V4R was seen in fourteen of the thirty cases and occurred between 0·05 and 0·07 second after the onset of the QRS complex in thirteen and at 0·04 second in one. It was therefore concluded that the occurrence of an embryonic R wave between 0·04 and 0·07 second after the start of the QRS complex in V1 and V4R may be within normal limits.

We thought it possible that the embryonic R wave in normal hearts might, with the development of right ventricular hypertrophy, sometimes increase in voltage until it became the secondary R wave of the RSR′ pattern or the R wave of right ventricular hypertrophy. With this in view, serial cardiograms of three patients over a period of up to 2½ years were examined, and it seemed that they did, in fact, lend support to this theory. Two cases were of the RSR′ pattern (Fig. 3 and 4)

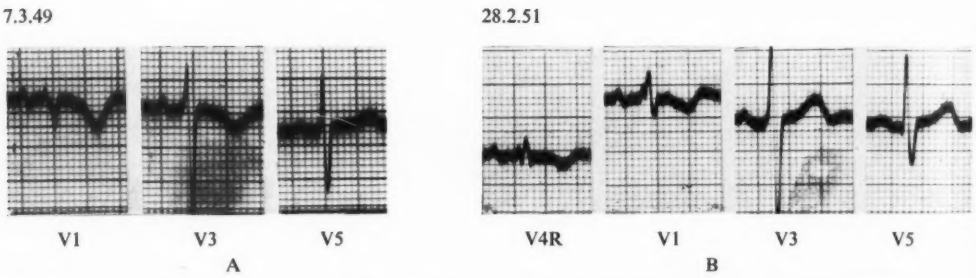

FIG. 3.—Selected chest lead cardiograms of case 22 illustrating the development of the RSR′ pattern. (A) Embryonic R wave in V1. (B) Secondary R wave in V1 and V4R. The time interval from the onset of the QRS complex to the peak of the embryonic R wave in tracing (A) and of the secondary R wave in tracing (B) is approximately the same (0·05 sec.).

and the third was an example of the pattern of right ventricular hypertrophy (Fig. 5). There was no good evidence that incomplete right bundle branch block contributed to the development of the RSR′ pattern in these two cases, since no essential difference in timing was noted between the secondary R waves and the original embryonic R waves from which they appeared to grow.

The close relationship between the cardiographic picture of right ventricular hypertrophy and the RSR′ pattern was further suggested in Case 20, Fig. 5. In serial graphs the mere disappearance of an initial R wave in right chest leads, which occurred concurrently with the growth of an embryonic R wave, changed the final picture from an RSR′ pattern to a QR pattern of right ventricular hypertrophy. Whether the presence or absence of an initial R wave in V1 is of sufficient functional significance to warrant a different ætiology being assigned to these two cardiographic patterns so strikingly similar in their progressive development, is questionable.

These theoretical considerations receive support in the high incidence of the RSR′ pattern found in proven cases of right ventricular hypertension and hypertrophy. Myers *et al.* (1948) in an analysis of the cardiograms of forty cases of right ventricular hypertrophy, proven at autopsy, found ten examples of the RSR′ pattern in addition to twenty showing the pattern of right ventricular hypertrophy. They considered that a persistent RSR′ pattern was suggestive, although not

* An embryonic R wave here denotes an upward deflection, the peak of which lies below or upon the isoelectric line.

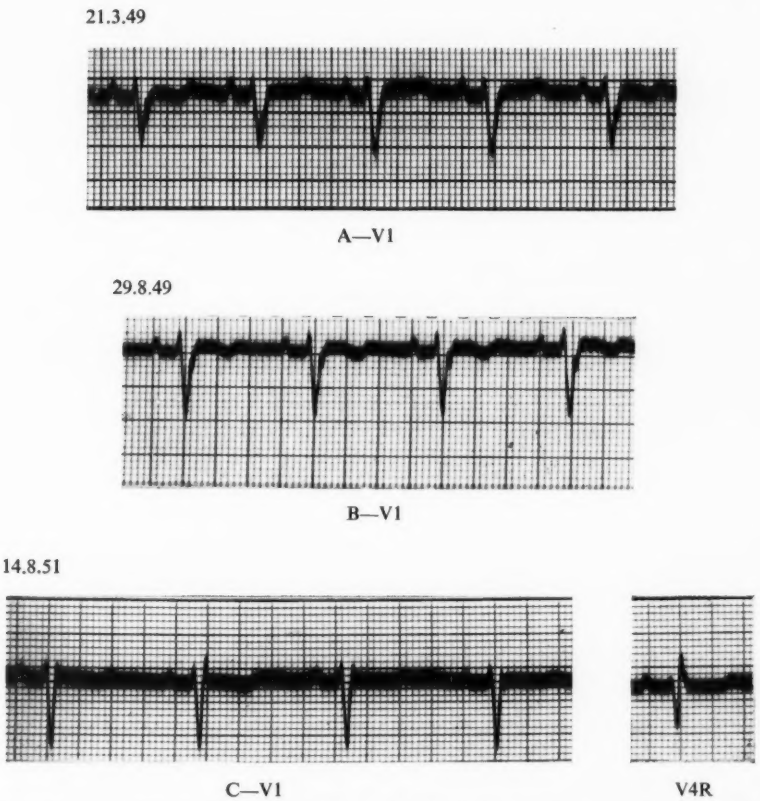

FIG. 4.—Selected chest lead cardiograms of case 8, illustrating the development of the RSR′ pattern. (A) and (B) Small embryonic R waves in V1. Their amplitude varies in phase with respiration. (C) Secondary R wave in V1 and V4R. The time interval from the onset of the QRS complex to the peak of the embryonic R wave in tracings (A) and (B) and of the secondary R wave in tracing (C) is approximately the same (0·07 sec.).

diagnostic, of right ventricular hypertrophy; they noted that it was usually transient when due to myocardial infarction or to pulmonary embolism. Johnson *et al.* (1950), in a series of forty cases of chronic pulmonary disease in whom right ventricular pressures had been measured, found seven examples of an RSR′ pattern. Four of these had high mean pulmonary artery pressures, two had moderately raised pressures, and in only one was the pressure normal. In our series four cases out of sixteen showed this pattern at the time of catheterization and a fifth subsequently developed it. All five showed raised right ventricular systolic pressures in the absence of cardiac failure. A high incidence of the RSR′ pattern in chronic pulmonary heart disease has also been noted by Thomas (1948), Lavenne (1951), and Kilpatrick (1951).

It is not suggested that every case with an RSR′ pattern has right ventricular hypertrophy. Friedland *et al.* (1947) found right ventricular hypertrophy in only 70 per cent of a series of cases with such a pattern. An RSR′ pattern is known to occur in normal hearts. But it would seem from the evidence presented that a persistent RSR′ pattern in cases of emphysema, is presumptive, although not pathognomonic, evidence of right ventricular hypertrophy.

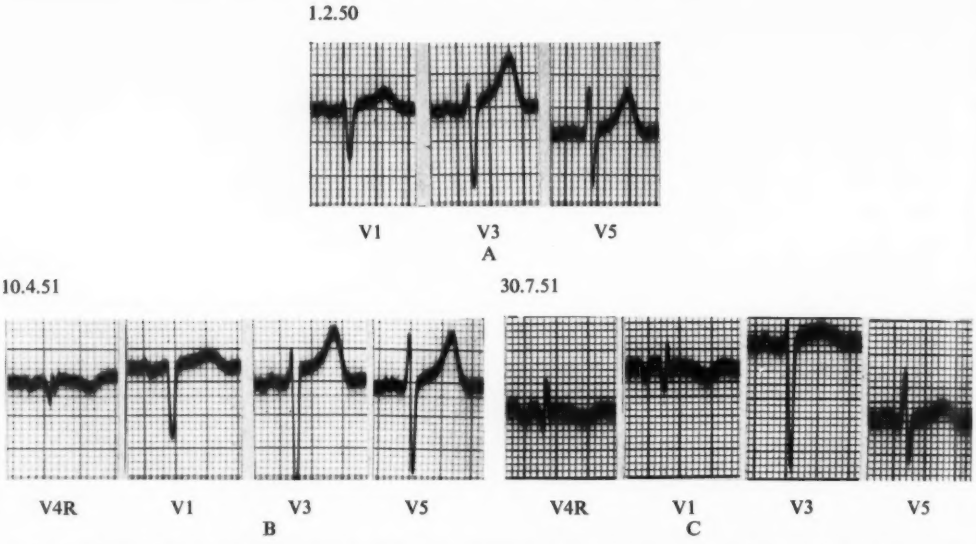

FIG. 5.—Selected chest lead cardiograms of Case 20, illustrating the development of right ventricular hypertrophy. (A) No embryonic R wave in V1. (B) Embryonic R wave in V1 and V4R. (C) Final R wave in V1 and V4R. The initial R wave in V1 seen in tracing (A) has disappeared, with the resultant QR complex in tracing (C). The time interval from the onset of the QRS complex to the peak of the embryonic R wave in tracing (B) and of the final R wave in tracing (C) is approximately the same (0·05 sec.).

DISCUSSION

Relationship of Cardiogram to Right Ventricular Pressure

The relationship between the cardiogram and resting right ventricular systolic pressure of patients not in failure was considered of interest since the findings of a raised pressure might be used as indirect evidence of right ventricular hypertrophy. It is likely that a greater degree or incidence of right ventricular hypertrophy may be found in patients with a sustained rise in resting right ventricular pressure when not in failure than in those in whom pulmonary hypertension is only intermittent. It will be seen from Fig. 6 that of the seven patients with resting right ventricular systolic pressures below 40 mm. Hg, six showed no cardiographic evidence of right ventricular hypertrophy while one had an RSR′ pattern, that was persistent. Of the nine patients with systolic pressures of 40 mm. Hg and above, two had cardiographic evidence of right ventricular hypertrophy, three of a persistent RSR′ pattern, one of complete right bundle branch block, and in three the cardiogram was normal. If a persistent RSR′ pattern in severe pulmonary emphysema be considered presumptive evidence of right ventricular hypertrophy, then some relationship is seen in the group as a whole between the cardiographic pattern and resting right ventricular systolic pressures in the absence of failure.

It will be noted, however, that the relationship was not a close one and that right ventricular hypertension occurred in some cases in the presence of a normal cardiogram. Cardiographic evidence of right ventricular hypertrophy, on the other hand, did not occur in the presence of a normal right ventricular pressure.

While our findings are in general agreement with those of Johnson *et al.* (1950), the two series cannot be very closely compared, since in their study the cardiograms were correlated with mean pulmonary artery pressures, as compared with systolic right ventricular pressures in our study;

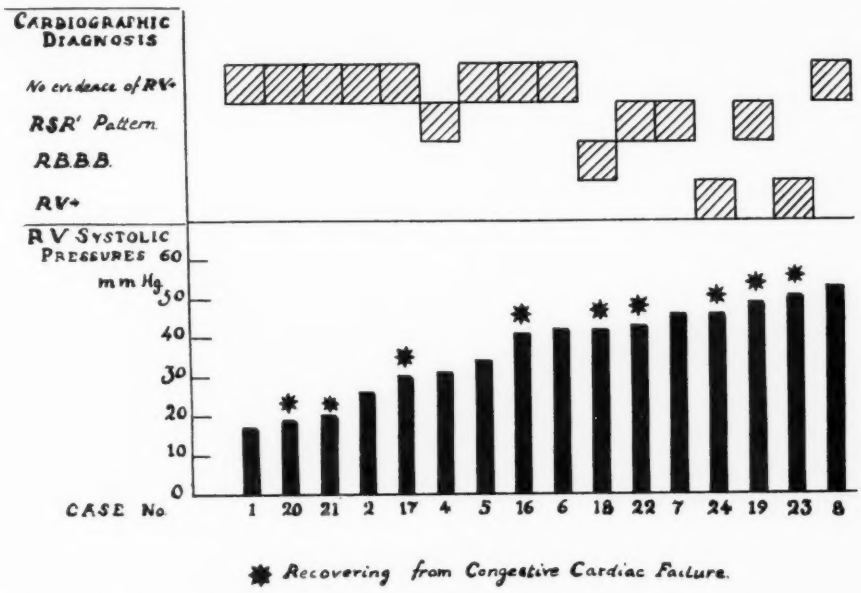

FIG. 6.—Relationship between the cardiogram and resting right ventricular systolic pressures of sixteen cases of severe pulmonary emphysema when not in cardiac failure.

in addition in some of their subjects in the high pressure group, the cardiograms were related only to the high pressures associated transiently with congestive heart failure. Similarly, close comparison of our findings to those of Kilpatrick (1951) is difficult, since he too used mean pulmonary arterial pressures (saline manometry) and did not distinguish between those patients who were and those who were not in congestive heart failure.

No immediate cardiographic alterations were found to accompany the marked fall in right ventricular systolic pressure, which was recorded on recovery from failure in the five patients in our series, in whom cardiac catheterization was repeated both in cardiac failure and on recovery from failure. In several of the patients, however, reported by Johnson *et al.* (1950), some cardiographic alterations did occur with the fall in mean pulmonary artery pressure on recovery from heart failure. In one case a QR pattern in V1 changed to an RSR′ pattern; simultaneously in lead V5 an RS changed to a QR pattern. These alterations were thought to be due to variations in the " electrical position " of the heart.

Relationship of the Cardiogram to the Onset of Cardiac Failure

In our series the onset of congestive failure anticipated the development of cardiographic evidence of right ventricular hypertrophy in five out of ten cases. The cardiogram remained negative in two out of four cases having a second attack of congestive failure. In one (Fig. 5), the cardiogram only became positive at the time of the seventh attack of cardiac failure over a period of twenty-one months. In two cases only did cardiographic evidence of right ventricular hypertrophy anticipate heart failure. It is therefore concluded that the development of cardiographic evidence of right ventricular hypertrophy may often be a late event in the clinical course of emphysema heart disease.

Summary

The cardiograms have been analysed in sixteen cases of severe pulmonary emphysema, in whom right ventricular pressures were measured. The cardiographic criteria for right ventricular hypertrophy have been based on those of Myers *et al.* (1948).

The genesis and possible significance of the RSR′ pattern in right chest leads in emphysema have been discussed and previous studies have been briefly reviewed. It was concluded that a persistent RSR′ pattern in pulmonary emphysema was presumptive, although not diagnostic, evidence of right ventricular hypertrophy.

The relationship between the cardiographic pattern and right ventricular pressures has been examined. In the series as a whole, a relationship was seen between cardiographic evidence of right ventricular hypertrophy and increased resting right ventricular systolic pressure in the absence of congestive cardiac failure.

It was shown, however, that right ventricular hypertension could occur in the presence of a normal cardiogram, although cardiographic evidence of right ventricular hypertrophy was not found in the presence of a normal pressure.

The development of cardiographic evidence of right ventricular hypertrophy, as here defined, was often a relatively late event in the clinical course of emphysema heart disease. The value of the cardiogram, therefore, appeared to lie more in confirming the nature of the heart disease present than in diagnosing its inception.

We wish to acknowledge with sincere thanks the help of Professor J. McMichael, under whose guidance this study has been carried out, and the assistance of other members of the staff who performed some of the cardiac catheterizations. We are indebted to Dr. W. A. Briscoe and Dr. G. A. McLemore for kindly supplying us with the respiratory data.

References

Bayliss, R. I. S., Etheridge, M. J., Hyman, A. L., Kelly, H. G., McMichael, J., and Reid, E. A. S. (1950). *Brit. Heart J.*, **12**, 317.

Borden, C. W., Wilson, R. H., Ebert, R. V., and Wells, H. S. (1950). *Amer. J. Med.*, **8**, 701.

Ferrer, M. I., Harvey, R. M., Cathcart, R. T., Webster, C. A., Richards, D. W., Jr., and Cournand, A. (1950). *Circulation*, **1**, 161.

Friedland, C., and Sodi-Pallares, D. (1947). *Arch. Inst. Cardiol.*, Mexico, **17**, 293.

Harvey, R. M., Ferrer, M. I., Richards, D. W. Jr., and Cournand, A. (1951). *Amer. J. Med.*, **10**, 719.

Johnson, J. B., Ferrer, M. I., West, J. R., and Cournand, A. (1950). *Circulation*, **1**, 536.

Kilpatrick, J. A. (1951). *Brit. Heart J.*, **13**, 309.

Lavenne, F. (1951). *Rev. belge. Path.*, 21, Suppl. 6.

Mounsey, J. P. D., Ritzmann, L. W., Selverstone, N. J., Briscoe, W. A., and McLemore, G. A. (1952). *Brit. Heart J.*, **14**, 153.

Myers, G. B., Klein, H. A., and Stofer, B. E. (1948). *Amer. Heart J.*, **35**, 1.

Thomas, A. J. (1948). *Brit. Heart J.*, **10**, 282.

Wilson, F. N., Rosenbaum, F. F., and Johnston, F. D. (1947). *Advances in Internal Medicine. New York Interscience Publications*, **2**, 1.

THE CARDIOGRAPHIC DIAGNOSIS OF COMBINED VENTRICULAR HYPERTROPHY

BY

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The introduction of unipolar lead cardiography has renewed interest in the cardiographic diagnosis of biventricular hypertrophy or strain. East and Bain (1948) stated that this diagnosis could often be made with the help of unipolar leads, but recent studies by Garouso *et al.* (1949), Soulié *et al.* (1949), Rosenman *et al.* (1950), and Levine and Phillips (1951) do not entirely support this view. The following investigation was undertaken to determine the frequency of cardiographic findings in this condition and, if possible, to establish reliable criteria for the diagnosis.

Case Material and Methods

Three groups were studied: Group I—26 patients with isolated right ventricular hypertrophy; Group II—30 patients with isolated left ventricular hypertrophy; and Group III—51 patients with right and left ventricular hypertrophy. Autopsy confirmation was obtained in all cases and unipolar as well as standard bipolar leads were recorded in all, using a Vector photographic machine and a Sanborn " Visocardiette " direct-writing instrument. Unipolar limb and chest leads were recorded by the technique of Goldberger (1947) (1 cm.=1·5 mv. for limb leads. 1 cm.=1 mv. for chest leads). The standard limb leads have been omitted from the analysis since they did not contribute any information not obtainable from a study of the unipolar leads. All age groups were represented. Cases of ischæmic heart disease, cardiac infarction, or cardiac aneurysm were excluded. Right bundle branch block was present in 3 cases in Group III, and left bundle branch block in 4 cases in Group II and 4 cases in Group III; these cases were excluded from the analysis of cardiographic signs, but were retained in the series as a whole.

Ætiology and Pathological Criteria of Ventricular Hypertrophy

All the common causes of heart disease were found, the most frequent being: in Group I pulmonary heart disease ; in Group II, hypertension; and in Group III, combined aortic and mitral valve lesions, and pulmonary heart disease associated with systemic hypertension.

Three degrees of hypertrophy were recognized. For the right ventricle, a thickness of the wall of 5 to 7 mm. was denoted by +, 8 to 10 mm. by ++, and more than 10 mm. by +++; for the left ventricle, 15 to 18 mm. was denoted by +, 19 to 24 mm. by ++, and more than 24 mm. by +++. In the few cases in which the wall was not measured in millimetres, an assessment was made in keeping with the above criteria, and based on the weight of the heart. Measurements were made at the outflow tract region of the right ventricle, the maximum muscle thickness being recorded, in both ventricles.

Cardiographic Criteria of Ventricular Hypertrophy

The features of isolated hypertrophy of the left or right ventricle respectively which were studied have been based on criteria used in this department and on work by Goldberger (1947), Sokolow and Lyon (1949), and Myers (1948 and 1950). The findings indicative of hypertrophy of both ventricles in Group III were derived from these criteria.

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Right Ventricular Hypertrophy. The following features were studied.

In V1. (1) Ventricular activation time greater than 0·03 of a second measured from the onset of the QRS to the peak of the R wave. (2) R wave greater than S; monophasic R wave or qR pattern. (3) Inversion or flattening of the T wave.

In V5. R wave smaller than S, indicating clockwise rotation of the heart around the longitudinal axis.

In aVR. (1) R wave greater than Q, indicating clockwise rotation round the long axis or backward rotation of the apex. (2) R wave greater than S. (3) Monophasic R wave.

A pointed P wave more than 2·5 mm. in amplitude in lead V1, suggesting auricular hypertrophy.

Vertical heart as shown by qR pattern or tall R wave in aVF with rS or QS in aVL.

Of these features, only the increase in ventricular activation time and the presence of a larger R than S wave in lead V1 can be considered direct signs. An R wave smaller than S in V5, and a predominantly positive deflection in aVR are indirect signs indicative of extreme clockwise rotation of the heart around its vertical axis, or backward apical rotation, which in our opinion is virtually diagnostic of right ventricular hypertrophy in the absence of cardiac infarction, ventricular aneurysm, or right bundle branch block. The presence of an R wave greater than Q in aVR is thought to be a particularly valuable indirect sign especially in children (Goodwin, 1952). An augmented P wave in V1 suggests auricular hypertrophy and is likewise an indirect sign. A vertical position of the heart may occur in normal persons and is not in itself a sign of right ventricular hypertrophy, although frequently associated with it. This criterion has been included for comparison with changes in heart position found in Groups II and III.

Left Ventricular Hypertrophy. The following features were studied.

In V5. (1) Ventricular activation time greater than 0·05 of a second except when the S wave was larger than the R. (2) R wave greater than 20 mm., or, together with S wave in V1, greater than 35 mm. (3) S–T segment depression greater than $\frac{1}{2}$ mm. and low voltage T wave in relation to high voltage R wave. (4) Flattening or inversion of the initial portion or the whole of the T wave.

In V1. S wave, together with R wave in V5, greater than 35 mm.

In aVL. *When the heart is horizontal and the left arm faces the left ventricle;* R wave greater than 11 mm. if S–T and T wave changes are absent. S–T segment depression of more than $\frac{1}{2}$ mm. Flattening, low voltage or inversion of all or initial portion of the T wave.

In aVF. *When the heart is vertical and the left leg faces the left ventricle;* R wave 20 mm. or more, S–T segment depression and T wave inversion. (Since these changes may occur in gross right ventricular hypertrophy, they cannot be assumed to indicate left ventricular hypertrophy unless associated with evidence of left ventricular hypertrophy in the præcordial leads. Furthermore, as will be seen later, the combination of vertical heart and left ventricular hypertrophy suggests combined hypertrophy.)

S–T segment depression and T wave inversion in leads facing the left ventricle were not accepted as evidence of left ventricular hypertrophy if digitalis had been administered, unless high voltage of R was also present.

Results

Fig. 1 shows that there are two striking differences between Groups I and II.

First, in aVL tall R and S–T depression, increase in voltage of the R wave in V5 and S wave in V1 did not occur in Group I.

Secondly, increase in ventricular activation time in V1, with R wave greater than S, and R smaller than S in V5, did not occur in Group II.

P wave taller than 2·5 mm., in V1 was seen in 3 cases of right ventricular hypertrophy and 3 cases of hypertrophy of both ventricles, but did not occur in isolated left ventricular hypertrophy.

Vertical position of the heart was present in two cases in Group II. One of them had an R wave larger than Q in aVR, associated with pathological evidence of isolated left ventricular hypertrophy. This case merits further attention and will be briefly described.

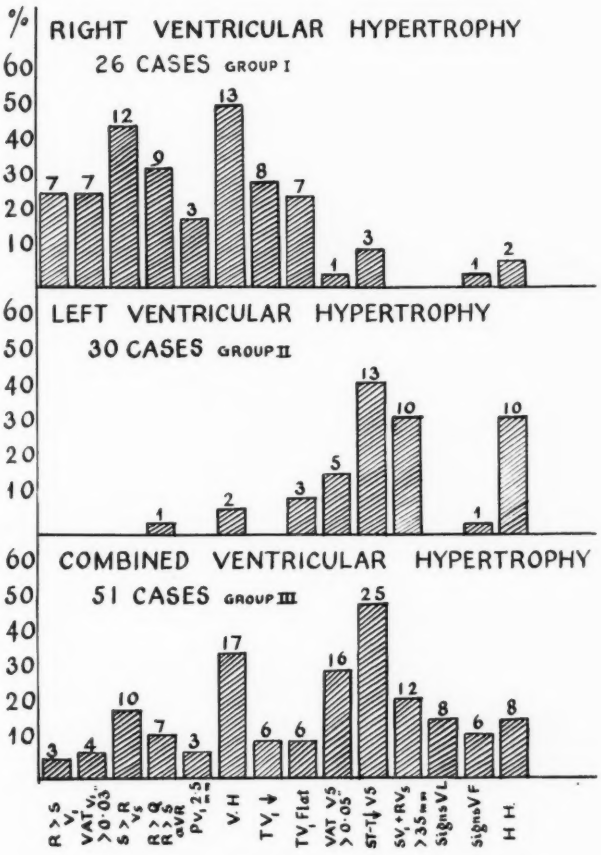

FIG. 1.—Frequency of cardiographic criteria of ventricular hypertrophy in the three groups studied.

The patient (J.P.) was a girl of 14 years, suffering from subacute nephritis, hypertension and uræmia with pericarditis. The initial electrocardiogram (Fig. 2) showed T waves suggestive of hyperkalæmia but no evidence of ventricular hypertrophy. Shortly before death, she developed left ventricular failure, pulmonary œdema, and pleural effusions. A further cardiogram, 24 hours before death (Fig. 3) showed slight evidence of left ventricular hypertrophy in the form of R greater than 20 mm. in V5. There was inversion of the initial portion of the T wave in V5, which could be ascribed to digitalis. In addition, a large R wave in aVR (Q/R ratio, 0·6) indicating backward rotation of the apex, strongly suggested dilatation of the right ventricle. Autopsy revealed isolated left ventricular hypertrophy, considerable pulmonary œdema, pleural effusions, and pericarditis. Presumably engorgement in the pulmonary circulation affected the right ventricle, resulting in the cardiographic features described.

In Group I, the ventricular activation time was greater than 0·05 seconds in 4 per cent, and ST–T segment changes were seen in 11 per cent, of cases in V5, but in no case was the sum of the R in V5

and S in V1 greater than 35 mm. A tall R and S–T depression in aVF was noted in 4 per cent and a horizontal heart position in 8 per cent of cases.

In Group I, 10 cases, which had varying degrees of right ventricular hypertrophy at autopsy, showed cardiographic features indicating extreme clockwise rotation of the heart around the long

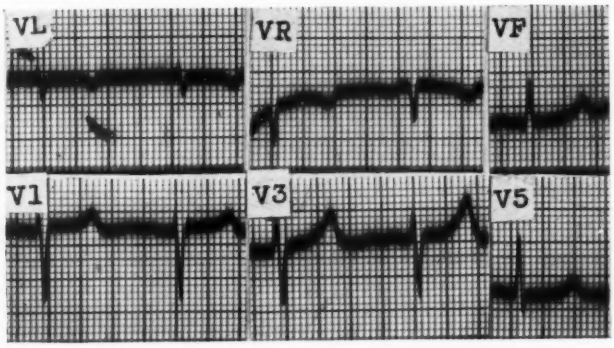

FIG.2.—*Case J.P., aged* 14. Subacute nephritis and uræmia. Cardiogram showing peaked T waves, but no signs of ventricular hypertrophy.

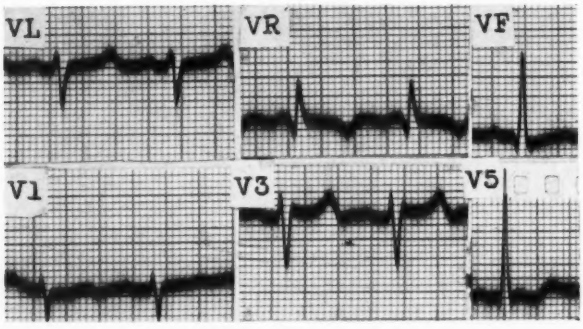

FIG. 3.—*Case J.P.* 24 hours before death from left ventricular failure and pulmonary œdema. Cardiogram now shows some evidence of left ventricular hypertrophy, RV5 = 20 mm., (+) inversion of initial portion of T wave, flat T in VF. In addition, tall R in aVR (Q/R ratio, 0·6) suggesting right ventricular involvement. Autopsy revealed isolated left ventricular hypertrophy (wall of left ventricle=16 mm.) but considerable pulmonary œdema and pleural effusions. Terminal right ventricular dilatation produced by left ventricular failure caused rotational changes.

axis, but no direct features of right ventricular hypertrophy. By contrast, in Group II, 3 cases that had an increase in voltage of SV1 and RV5 without S–T segment or T wave abnormalities were found to have moderate degrees of left ventricular hypertrophy at autopsy.

In Group III, signs of left ventricular hypertrophy predominated over those of right ventricular hypertrophy, while the frequency of a vertical position of the heart was slightly less than in Group I but much greater than in Group II. Direct signs of right ventricular hypertrophy were infrequent,

although indirect signs were more common. An R wave smaller than S in V5 occurred in approximately the same number of cases in Groups I and III, but this sign was absent in Group II. R wave larger than Q in aVR was not seen in Group II, with the exception of *Case J.P.* already described. Inversion of the T wave in V1 was noted most frequently in Group I, but never in Group II.

The cardiographic diagnoses in individual cases in Group III are shown below.

Cardiographic evidence	*No. of Cases*
Combined hypertrophy	13
Isolated left ventricular hypertrophy	13
Isolated right ventricular hypertrophy (direct)	3 } 10
" " " " (indirect)	7 }
Pure left bundle branch block	4 } 6
Pure right bundle branch block	2 }
Intraventricular block	1
Non-specific	8
Total	51

Seventy per cent of cases showed some signs of ventricular hypertrophy, and bundle branch block was present in 6 cases. Of these 70 per cent, signs of isolated left ventricular hypertrophy or combined hypertrophy occurred more frequently than signs of right ventricular hypertrophy.

Fig. 4 is an example of cardiographic signs of pure left ventricular hypertrophy in a patient with gross (+++) left ventricular and moderate (++) right ventricular hypertrophy at autopsy. By contrast, Fig. 5 and 6 illustrate two cases with signs of pure right ventricular hypertrophy, both of which had much right ventricular and slight left ventricular hypertrophy at autopsy. Both these tracings show a prominent R wave in aVR which in Fig. 5 is larger than Q. The S–T segment depression in this cardiogram is due to digitalis.

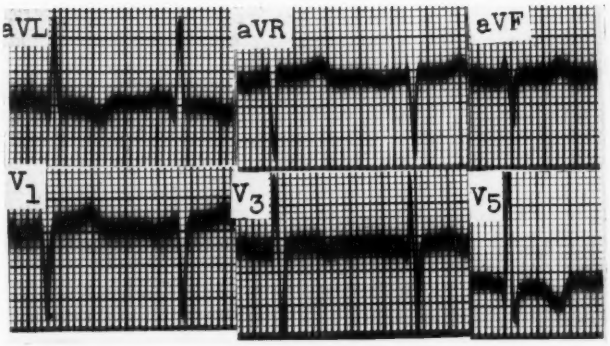

FIG. 4.—Cardiographic evidence of pure left ventricular hypertrophy in a patient with combined hypertrophy due to aortic incompetence and chronic bronchitis and emphysema. (Diameter of left ventricular wall=25 mm. Diameter of right ventricular wall=8 mm.) Cardiogram shows horizontal heart, high voltage of R wave in V5 and aVL, sharp inversion of T wave in V5, aVL.

Table I gives a detailed analysis of 13 cases in which the cardiographic signs were suggestive of combined hypertrophy. Evidence of left ventricular hypertrophy predominated in all these cases and was associated with vertical position of the heart in 7 (Fig. 7, 8, and 12). Case 1 (Fig. 9) showed

high voltage of R and S–T segment depression with inversion of initial portion of the T wave in V5, in association with a vertical heart. These features were due to left ventricular hypertrophy

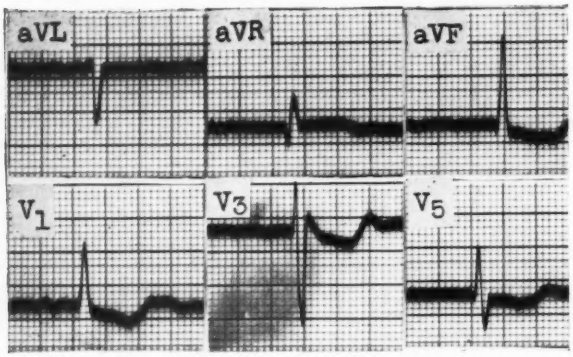

FIG.5.—Signs of pure right ventricular hypertrophy in a patient with combined ventricular hypertrophy due to rheumatic carditis. At autopsy, gross right ventricular hypertrophy and slight left ventricular hypertrophy were present.

The cardiogram shows clockwise rotation round the long axis, monophasic R in V1 (ventricular activation time, 0·04/sec.), qR in aVR (Q/R ratio, 0·4). S–T segment depression. The inversion of T waves cannot be ascribed to left ventricular hypertrophy, since digitalis had been given. Auricular fibrillation is present.

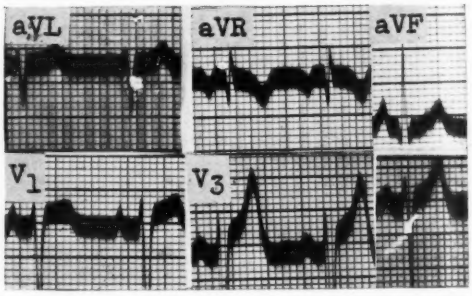

FIG. 6.—Signs of pure right ventricular hypertrophy in a patient with combined hypertrophy (hypertension, bronchitis and emphysema). At autopsy, marked right ventricular hypertrophy (diameter of wall, 10 mm.) and slight left ventricular hypertrophy (17 mm.). Gross clockwise rotation round the long axis, prominent R wave in aVR (Q/R ratio=1), S wave greater than R in V5.

although the S–T segment depression might have been partly the result of digitalis. At autopsy, gross left ventricular hypertrophy and slight right ventricular hypertrophy were found.

An S wave larger than R in V5 indicative of extreme clockwise rotation round the long axis due to right ventricular hypertrophy in Cases 3 and 4 (Fig. 10) was not present in any subject with isolated left ventricular hypertrophy. An S wave larger than R in V5 associated with cardiographic signs of left ventricular hypertrophy and horizontal position of the heart was therefore considered one of the diagnostic patterns of combined hypertrophy.

In Case 2, the large R wave in aVR associated with large P waves and signs of left ventricular hypertrophy is also evidence of hypertrophy of both ventricles (Fig. 11). An R wave greater than Q in aVR was never found with isolated left ventricular hypertrophy, except in J.P., in whom the large R wave was produced by terminal dilatation of the right ventricle, secondary to left ventricular failure. The T wave in V1 was flat in Case 8, and inverted in Cases 11, 12, and 13. The inversion of T in V1, associated with signs of left ventricular hypertrophy, may be accepted as evidence of combined hypertrophy, since it was not seen in any case in which the left ventricle was hypertrophied alone. By contrast, a flat T in V1 was seen in 3 cases of isolated left ventricular hypertrophy, so that its occurrence in Cases 11 and 12, which had no evidence of right ventricular hypertrophy, cannot be assumed to indicate enlargement of the right ventricle.

The relative degree of hypertrophy of either ventricle was not linked to cardiographic signs of hypertrophy of both ventricles. Cardiographic changes due to clockwise rotation round the long

TABLE I

TABLE I

Case	Age	Clinical Diagnosis	Degree of Ventricular Hypertrophy		V1 R/S>1 (R>S)	V1 VAT >0·03 sec.	V5 R/S<1 R<S)	aVR R/S>1 R/Q>1 R>Q	P >2·5 mm.	Vertical heart	V1 T↓	V5 VAT >0·05 sec.	V5 ST–T↓	Volt SV1 + RV5 =35 mm. or more	Signs in aVL	Signs in aVF	Hori-zontal heart
			L.	R.													
1	49	Cor pulmonale Hypertension	++	+	–	†	–	–	–	†	–	†	†	–	–	–	–
2	69	Aortic stenosis Hypertension	++	+ dil.	§	§	–	†	†	–	–	†	†	–	†	–	†
3	75	Mitral stenosis Aortic stenosis Aortic incompetence	++	+ dil.	–	–	†	–	§	–	–	–	†	–	†	–	†
4	47	Hypertension Congestive cardiac failure Uræmia	++	+ dil	–	–	†	–	–	–	–	–	†	–	†	–	†
5	49	Mitral stenosis Mitral incompetence Aortic incompetence Tricuspid incompetence	+	+	§	§	–	–	§	†	–	–	†	–	–	†	–
6	52	Hypertension Congestive cardiac failure	+	+	–	–	–	§	–	†	–	†	†	†	–	†	–
7	63	Hypertension	++	+	–	–	–	§	–	†	–	†	†	–	–	–	–
8	58	Chronic bronchitis Emphysema Chronic nephritis	++ dil.	+ dil.	–	–	–	–	–	†	flat	–	†	†	–	†	–
9	64	Mitral stenosis Aortic stenosis Aortic incompetence	++	+	–	–	–	–	–	†	–	†	†	†	–	†	–
10	59	Mitral stenosis	+	++ dil.	–	–	–	–	§	†	–	–	†	–	–	†	–
11	29	Aortic incompetence Mitral stenosis Subacute bacterial endocarditis Nephritis	++ dil.	+	–	–	–	–	–	–	flat	–	†	–	†	–	†
12	80	Emphysema	++	+ dil.	–	–	§	§	–	–	flat	†	†	†	–	–	–
13	77	Aortic stenosis Mitral stenosis	++	+++ dil.	–	–	§	–	–	–	†	†	†	–	–	–	–

VAT=Ventricular activation time. † =Present. ↓=Inverted. §=Could not be measured. dil.=Dilated.

axis of the heart suggesting right ventricular hypertrophy were present in those cases with dilatation of the right ventricle at autopsy. It is therefore likely that dilatation may cause rotation of the heart in these circumstances, as in pulmonary embolism.

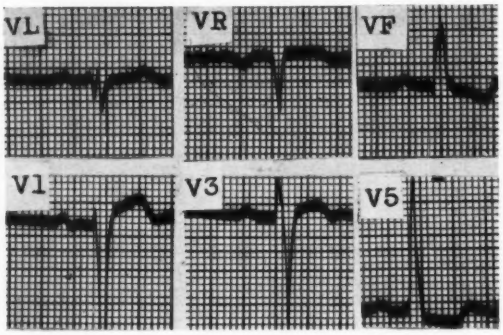

FIG. 7.—*Case* 6, *Table I.* Signs of left ventricular hypertrophy with vertical heart in a patient with combined hypertrophy of unknown ætiology. (Autopsy: left ventricle wall, 17 mm. diameter; right ventricle, 7 mm.).

Cardiogram shows RV5 and SV1 greater than 35 mm., S–T depression in V5, inverted TVF. Absence of q in V5 indicates slight clockwise rotation or incomplete left bundle branch block due to left ventricular hypertrophy. S–T segment depression in V5 may be due to digitalis, but sharp T wave inversion in VF is probably a true sign of left ventricular hypertrophy.

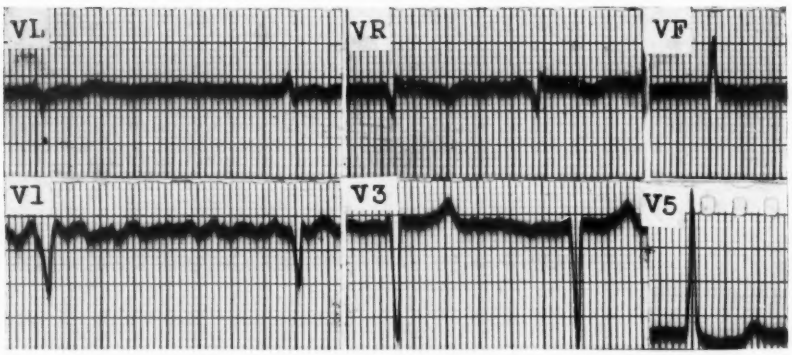

FIG. 8.—*Case* 5, *Table I.* Eveidence of left ventricular hypertrophy with vertical heart in a patient with bilateral hypertrophy due to rheumatic carditis. (Autopsy: left ventricular wall=17 mm.; right ventricular wall=6 mm. (10 mm. in outflow tract).

Cardiogram shows RV5=20 mm., S in V3=16 mm., vertical heart. S–T segment depression may be partly due to digitalis. Auricular fibrillation is present.

DISCUSSION

Only about one-quarter of the cases with hypertrophy of both ventricles is likely to show a characteristic cardiogram. In this series, normal curves occurred in 16 per cent, signs of isolated right ventricular hypertrophy in 20 per cent, signs of isolated left ventricular hypertrophy in 62

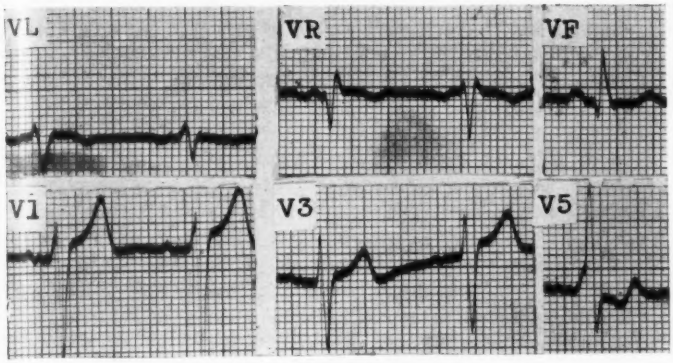

FIG. 9.—*Case* 1, *Table I.* Signs of left ventricular hypertrophy in vertical heart in a patient with bilateral hypertrophy due to cor pulmonale and hypertension. (Autopsy: marked left ventricular hypertrophy, slight right ventricular hypertrophy, with dilatation.)

Cardiogram shows vertical heart, RV5+SV1 greater than 35 mm., slurring of upstroke of R in V1 and V5, QRS duration, 0·14 sec. in V5. Inversion of initial portion of T in V5. Nodal rhythm.

per cent, bundle branch block in 12 per cent, and appearances suggestive of combined hypertrophy in the remainder.

The results show that evidence of combined hypertrophy may be of two types: (1) definite indications of associated right and left hypertrophy (which did not occur in cases of isolated hypertrophy of one or other ventricle only), and (2) probable indications, which, however, also occurred in a small number of cases of isolated hypertrophy of one or other ventricle respectively.

The definite features consisted of extreme clockwise rotation; S wave greater than R in V5 (2 cases), R wave greater than Q in aVR (1 case), T wave inversion in V1 (1 case), in conjunction with signs of left ventricular hypertrophy. Probable features were the association of left ventricular hypertrophy with vertical position of the heart (7 cases). Clockwise rotation of the heart on its long axis, in association with evidence of left ventricular hypertrophy, suggests that the enlarging right ventricle causes this rotation, possibly in displacing the left ventricle posteriorly. The direct signs of right ventricular hypertrophy, namely, increase in activation time of the right ventricle and R wave greater than S in V1, are masked by those of left ventricular hypertrophy. Dilatation of the right ventricle, which may increase the clockwise rotation, was present in 7 of the 13 cases with signs of hypertrophy of both ventricles.

These findings are in general agreement with those of Soulié *et al.* (1949) and Garouso *et al.* (1949). These workers all stress the importance of a combination of vertical heart or right axis deviation with evidence of left ventricular hypertrophy. Rosenman *et al.* (1950), referring only to cases of rheumatic heart disease, found that these criteria did not necessarily apply to cases of left ventricular hypertrophy due to other causes. But, post-mortem confirmation of hypertrophy of one or both ventricles was obtained in only two of their cases. It is of interest that Kaplan and Katz (1941), reviewing the cardiographic patterns of left ventricular hypertrophy, recalled the observation of Thomson and White (1936) that right ventricular hypertrophy is a common sequel to left ventricular hypertrophy.

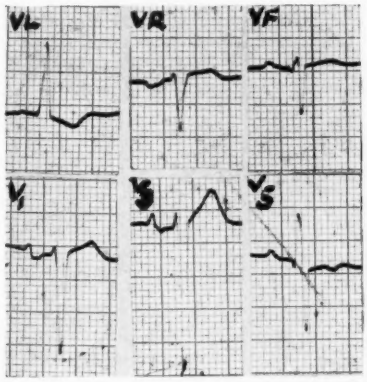

FIG. 10.—*Case* 4, *Table I.* Signs of left ventricular hypertrophy associated with extreme clockwise rotation round the long axis in a patient with bilateral hypertrophy due to hypertension. (Autopsy: left ventricle= 21 mm., right ventricle, 7 mm., right ventricle dilated.)

Cardiogram shows horizontal heart, R in VL=10 mm., S–T depression and T inversion in VL, clockwise rotation with deep S in V5, initial portion of TV5 inverted.

In the present series 5 of the 13 cases showing combined cardiographic features had lesions of mitral and aortic valves, while 3 cases had lone hypertension or aortic valve disease. Our results suggest that the ætiology of the ventricular hypertrophy does not influence the reliability of the cardiographic criteria. In two cases of isolated left ventricular hypertrophy, a vertical heart

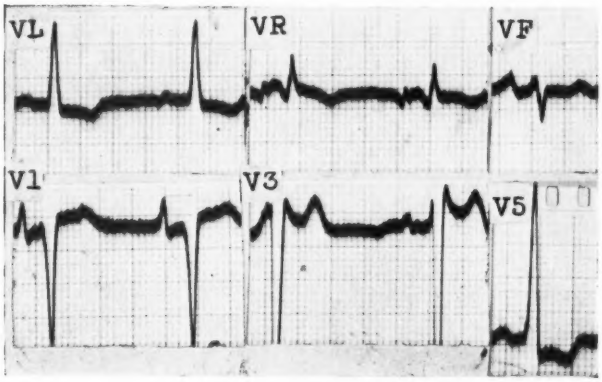

FIG. 11.—*Case* 2, *Table I.* Signs of right and left ventricular hypertrophy in a patient with bilateral hypertrophy associated with aortic stenosis and hypertension. (Autopsy: left ventricle, 20 mm., right ventricle, 7 mm., right ventricle dilated.)

Cardiogram shows horizontal heart, RV5+SV1 greater than 35 mm. T wave inversion in V5. Ventricular activation time greater than 0·05 sec. in V5. RaVL=12 mm. S–T depression in V5 and VL. qR in aVR (Q/R ratio=0·3). Augmented P in V1 (3 mm.).

position was associated with signs of left ventricular hypertrophy, and in both the cause of death was renal disease with hypertension. One of these (J.P.) showed cardiographic evidence of terminal right ventricular dilatation as a result of left ventricular failure, and the other had bronchitis during life. Terminal pulmonary engorgement may affect the right ventricle and produce cardiographic appearances that, when superimposed on the findings of hypertrophy of the left ventricle, provide evidence that both ventricles are enlarged.

It is possible that the presence of signs of combined hypertrophy may have some prognostic value in patients with lone aortic or hypertensive disease, as an indication of impending failure of the right ventricle. An R wave larger than Q in aVR, without evidence of right ventricular hypertrophy in V1, has not been mentioned by previous writers, but, as shown in our series, is of some value when present in association with the findings of left ventricular hypertrophy.

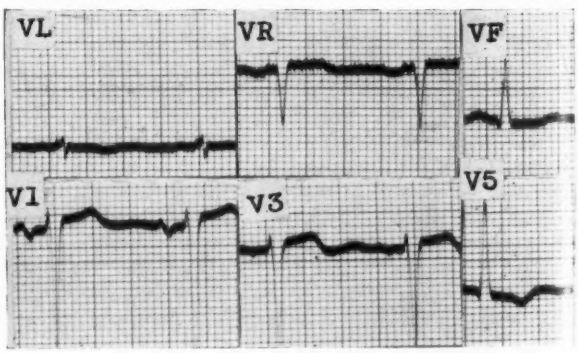

FIG. 12.—*Case* 7, *Table I.* Signs of left ventricular hypertrophy with vertical heart in a patient with bilateral hypertrophy due to hypertensive heart disease. (Autopsy: gross left ventricular hypertrophy, slight right ventricular hypertrophy.)

Cardiogram shows vertical heart, RV5+SV1=35 mm. or more, T wave inversion in V5, S–T segment depression in V5 and VL.

Whereas the presence of the signs of left ventricular hypertrophy in a vertical heart suggests enlargement of both ventricles, the combination of signs of right ventricular hypertrophy with horizontal heart does not provide evidence of combined hypertrophy.

Summary

Unipolar lead cardiograms have been studied in 51 patients with combined ventricular hypertrophy, 26 patients with isolated right ventricular hypertrophy, and 30 patients with isolated left ventricular hypertrophy. Autopsy confirmation was obtained in all cases. In the group with combined hypertrophy 13 subjects had signs of left ventricular hypertrophy only and 10 of right ventricular hypertrophy only. Right bundle branch block occurred in two, left bundle branch block in four, non-specific appearances in 8, and evidence of combined hypertrophy in 13 patients.

Direct evidence of right ventricular hypertrophy—increased ventricular activation time and R wave greater than S in V1—was masked by left ventricular hypertrophy. Seven of the 13 cases had features of left ventricular hypertrophy with a vertical heart, and this combination was considered strongly suggestive, but not absolutely diagnostic, of combined hypertrophy, since it was seen in two cases in the control group with isolated left ventricular hypertrophy. One of these cases was thought to have terminal acute right ventricular dilatation secondary to left ventricular failure.

A combination of features of left ventricular hypertrophy, with S wave greater than R in V5 occurred in two cases, and with R wave greater than Q in aVR, and enlarged P in V1, in one case. The association of these rotational signs of right ventricular hypertrophy was not seen in any case of left ventricular hypertrophy without right ventricular enlargement, and their association with signs of left ventricular hypertrophy was considered diagnostic of enlargement of both ventricles. In another case, signs of left ventricular hypertrophy occurred in combination with an inverted T wave in V1. This did not occur in any case of isolated left ventricular hypertrophy and was thought to indicate associated hypertrophy of the right ventricle.

It is concluded that cardiographic signs of combined hypertrophy are likely to be seen in only about one-quarter of cases in which there is hypertrophy of both sides. The association of a vertical heart with signs of left ventricular hypertrophy is highly suggestive of combined hypertrophy. The presence of an R wave greater than Q in aVR, S wave larger than R in V5 with inversion of T wave in V1, together with signs of left ventricular hypertrophy, is diagnostic of combined hypertrophy.

The presence of the cardiographic signs of right ventricular enlargement in addition to those of hypertrophy of the left ventricle due to a pure left-sided lesion may have some prognostic value. Dilatation of the right ventricle may be a cause of specific signs of rotation.

We wish to thank Dr. C. V. Harrison for permission to examine the post-mortem records, and for advice on pathological criteria.

Thanks are also due to Professor J. McMichael, Dr. Terence East, and Dr. David Lewes for advice and criticism.

References

East, T., and Bain, C. W. C. (1948). *Recent Advances in Cardiology*. Churchill, London.
Garouso, G., Deschamps, H., Tilmant, J., Lenegre, J., and Kalaidonis, P. (1949). *Arch. Mal. Cœur.* **42**, 711.
Goldberger, E. (1947). *Unipolar Lead Electrocardiography*. Henry Kimpton, London.
Goodwin, J. F., (1952). *Brit. Heart J.*, **14**, 173.
Kaplan, L. G., and Katz, L. N. (1941). *Amer. J. med. Sci.*, **201**, 676.
Levine, H. D., and Phillips, E. (1951). *New England J. Med.*, **245**, 837.
Myers, G. B. (1950). *Amer. Heart J.*, **39**, 637.
——, Klein, H. H., and Stofer, B. E. (1948). *Amer Heart J.*, **35**, 1.
Rosenman, R. H., Krause, S., Hwang, W., and Katz, L. N. (1950). *Amer. Heart J.*, **40**, 453.
Sokolow, M., and Lyon, T. P. (1) (1949). *Amer. Heart J.*, **37**, 161.
——, —— (2) (1949). *Amer. Heart J.*, **38**, 273.
Soulie, P., Laham, J., Papanicolis, I., and Voci, G. (1949). *Arch. Mal. Cœur.*, **42**, 791.
Thomson, W. P., and White, P. D. (1936). *Amer. Heart J.*, **12**, 641.

A COMPARISON OF UNIPOLAR LEADS OBTAINED WITH THE METHODS OF WILSON AND GOLDBERGER

BY

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Wilson *et al.* in 1934 introduced a method of obtaining unipolar leads representing the potential variations of a single electrode, by using as an indifferent electrode a central terminal that was obtained by connecting the lead wires of the three extremities through non-inductive resistances of 5000 ohms. It is assumed that this central terminal has a potential of zero, the assumption being based on Einthoven's equilateral triangle theory and Kirchoff's law. Although it has been shown (Dolgin *et al.*, 1949) that this central terminal is not a truly indifferent electrode and may show some potential, this method has proved to be the most practical one for obtaining unipolar leads.

Goldberger in 1942 introduced a modification of Wilson's method for obtaining unipolar limb leads by omitting the resistances between the extremities and the central terminal, and disconnecting the lead wire of the explored extremity from the central terminal. According to Goldberger, an amplification of 50 per cent of the potential of the corresponding Wilson unipolar limb lead is thus obtained.

Various studies (Bryant and Johnston, 1946; Bryant *et al.*, 1949; Griffeath and Sokolow, 1951) have been made, comparing the unipolar limb lead electrocardiograms taken by the method of Goldberger with corresponding curves taken after modifying this method by the introduction of 5000 ohm resistances between the limb electrodes and the central terminal. In these studies differences in the amplitude of the deflections were found in under 10 per cent of the cases. Kisch (1948) in one case compared the Goldberger unipolar limb leads with the corresponding Wilson limb leads and found that the ratio between them was inconstant, varying from limb to limb. Rappaport and Williams (1949) analysed the methods of Wilson and Goldberger from a theoretical mathematical point of view, and concluded that the Goldberger method gave better results when used with the Wilson central terminal.

We are reporting a comparative study between Wilson's unipolar limb leads (VR, VL, VF) and Goldberger's augmented unipolar limb leads (aVR, aVL, aVF). The purpose of the study is: to determine (1) whether the (assumed) 1:1·5 ratio between Wilson's leads and Goldberger's augmented leads is valid; and (2) whether there are differences in the form and direction of the deflections recorded by the two methods.

Method of study. Fifty patients showing abnormal cardiograms were studied. They were taken by a Cambridge string galvanometer, recording consecutively the three Wilson unipolar limb leads and the three Goldberger's augmented unipolar limb leads. In addition the three standard limb leads and the six unipolar præcordial leads (V1–V6) were taken. Special care was given to proper preparation of the skin. In every one of the 300 tracings, attention was paid to the standardization (1·0 MV=10 mm.). The waves of the ventricular complex, Q, R, S, and T were measured (a magnifying lens being used) in at least three consecutive cardiac cycles, and appropriate corrections were made for eventual errors in the standardization. The mean value of each wave in three consecutive cycles in Wilson's and Goldberger's leads were calculated and the ratio between them determined—VR/aVR, VL/aVL, and VF/aVF.

Results

The results are summarized in the table. The mean ratio between the corresponding waves recorded from the same limb with the two methods was found to be inconstant and to vary considerably. Thus, for example, the following results were obtained for the right arm: QaVR/QVR=1·51±0·22; RaVR/RVR=2·02±0·84; SaVR/SVR=1·56±0·09; TaVR/TVR=1·86±0·67. Except for very few instances, marked variations of this ratio were found from case to case, as may be seen from the wide spread of the limits of the true mean.

Furthermore, the mean ratio of the identical waves obtained from the different limbs was also found to show variations; for example, in the case of the R waves the following results were obtained: RaVR/RVR=2·02±0·84; RaVL/RVL=1·75±0·82; RaVF/RVF=1·65±0·45.

In two instances a significant discrepancy in the form of the waves was found. In the first an upright T of 0·4 mm. was seen in aVL, while it was isoelectric in VL; in the second a Q of 0·6 mm. was seen in aVL while it was absent in VL.

TABLE

Deflection	Leads	No. of observations	Mean of ratio	Standard deviation	Standard error of the mean	The true mean is likely to lie within the limits of
Q	AVR/VR	28	1·51	0·22	±0·04	1·4–1·6
Q	AVL/VL	20	1·93	0·87	±0·19	1·5–2·3
Q	AVF/VF	16	2·47	1·68	±0·42	1·6–3·3
R	AVR/VR	34	2·02	0·84	±0·15	1·7–2·3
R	AVL/VL	46	1·75	0·82	±0·12	1·5–2·0
R	AVF/VF	49	1·65	0·45	±0·06	1·5–1·8
S	AVR/VR	20	1·56	0·09	±0·02	1·5–1·6
S	AVL/VL	16	1·68	0·28	±0·07	1·5–1·8
S	AVF/VF	28	1·75	0·34	±0·07	1·6–1·9
T	AVR/VR	45	1·86	0·67	±0·10	1·7–2·1
T	AVL/VL	39	1·99	1·13	±1·18	1·6–2·4
T	AVF/VF	47	2·03	0·84	±0·12	1·8–2·3

Comment

As seen from the results the ratio between the waves of the ventricular complex obtained by the Wilson unipolar leads and the Goldberger augmented unipolar leads varies from lead to lead and from wave to wave. Thus the assumption that there is a constant ratio of 1:1·5 between the potentials recorded by Wilson's unipolar leads and Goldberger's augmented leads could not be verified in our series. The ratio of 1:1·5 was derived from calculations based on the concept of Enthoven's equilateral triangle, the heart being equidistant from each angle, and accordingly it was concluded that the central terminal of Wilson equals zero.

Goldberger modified the Wilson method by eliminating the 5000 ohms resistances and by disconnecting the electrode of the explored limb from the central terminal. With this procedure each extremity was coupled with a central terminal of a different potential, obtained by omitting a different angle of the triangle for each lead. This is in contrast with the Wilson method in which the same central terminal is used for each extremity. Furthermore, elimination of the 5000 ohm resistances from the central terminal may increase the distorting effect of inequalities in the skin resistances. These factors may account for the inconsistency and variations in the potentials recorded by the two methods in our series.

Summary

Wilson's and Goldberger's unipolar limb leads were compared in 50 cases with abnormal electrocardiograms.

The ratio between the potentials recorded by the two methods was found not to be 1:1·5. No constant relationship was found between the potentials recorded by the two methods, though the ratio generally lay between 1:1·5 and 1:2·0.

References

Bryant, J. M., and Johnston, F. D. (1946). *J. Clin. Invest.*, **25**, 919.
——, ——, and Wilson, F. N. (1949). *Amer. Heart J.*, **37**, 321.
Dolgin, M., Grau, S., and Katz, L. N. (1949). *Amer. Heart J.*, **37**, 868.
Goldberger, E. (1942). *Amer. Heart J.*, **23**, 483.
Griffeath, M. J., and Sokolow, M. (1951). *Amer. Heart J.*, **41**, 105.
Kisch, B. (1948). *Exper. Med. Surg.*, **6**, 1.
Rappaport, M. B., and Williams, C. (1949). *Amer. Heart J.*, **37**, 892.
Wilson, F. N., MacLead, A. G., and Barker, S. P. (1932). *Proc. Soc. Exper. Biol. Med.*, **29**, 1011.
——, Johnston, F. D., MacLead, A. G., and Barker, P. S. (1934). *Amer. Heart J.*, **9**, 447.

THE RESPONSE OF ARRHYTHMIAS AND TACHYCARDIAS OF SUPRAVENTRICULAR ORIGIN TO ORAL PROCAINE AMIDE

BY

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The introduction of procaine amide for the control of cardiac arrhythmias in man has been recent (Mark *et al.*, 1950). There are relatively few reports at present concerned with it. Those published have dealt chiefly with the use of the preparations of the drug given by intravenous injection and have emphasized its value in arrhythmias of ventricular origin (Mark *et al.*, 1950; Joseph *et al.*, 1951; Garlett *et al.*, 1951; Kinsman *et al.*, 1951; Miller *et al.*, 1951; Kayden *et al.*, 1951; and Stearns and Callahan, 1951). Thus, it has been stated that procaine amide is of value in ventricular arrhythmias but that its effect " on auricular function appears to be minimal " (Joseph *et al.*, 1951).

With the advent of the preparation for use by mouth,* a study of the action of orally administered procaine amide upon supraventricular disturbances of the heart beat was undertaken.

Material and Methods

This report is based upon observations of 100 instances of supraventricular arrhythmias or tachycardias which occurred in 83 patients in the Beth Israel Hospital during the past year and a half, admitted because of organic heart disease. None were patients under anæsthesia for surgery. All were between 25 and 75 years of age, the majority being between 40 and 60 years. The sex distribution was approximately equal.

The drug, procaine amide, was given by mouth, and according to the following schedule.

A test dose of 250 mg. was followed in one hour by a 1-g. oral dose. Thereafter, 1 g. every four hours was administered. If, after 5 g. of the drug had been given, the arrhythmia had not been abolished, the drug schedule was changed to 1 g. every three hours.

In all cases the drug was continued until the arrhythmia was abolished or some toxic effect occurred. Following the restoration to sinus rhythm, the dosage was gradually reduced over the course of the succeeding forty-eight hours to 0·5 g. every six hours.

In those subjects in whom the arrhythmia could not be abolished with procaine amide, a course of oral quinidine sulphate, 0·4 g. every two hours was undertaken. The quinidine was also given until the arrhythmia was converted or toxic effects produced.

In several instances following restoration of sinus rhythm by means of procaine amide, the drug was withdrawn, the arrhythmia allowed to recur and procaine amide again administered with restoration of sinus rhythm.

* Supplied as pronestyl hydrochloride by E. R. Squibb & Co.

Results

Many supraventricular arrhythmias responded to procaine amide. In these patients, neither the type of heart disease nor the presence of digitalis medication influenced the action of procaine amide significantly. The most important factors were the type and duration of the arrhythmia.

Auricular Fibrillation. The cases of auricular fibrillation have been considered in three groups: (A) those subjects in whom the auricular fibrillation was of less than one week's duration; (B) those in whom the auricular fibrillation was of longer than one week's duration but clearly less than three years; and (C) those in whom auricular fibrillation had been present for three years or longer.

Group A. There were 21 patients with auricular fibrillation of less than one week's duration. Restoration of sinus rhythm with procaine amide occurred in 17. Conversion occurred in two instances after only 1·25 g. of the drug had been taken. In most instances, however, it required 3 to 4 g. for conversion. In the four instances of failure to correct the arrhythmia, quinidine also failed to secure reversion to normal sinus rhythm. No significant toxicity to the drug was observed in this group.

Group B. There were 25 patients whose fibrillation was of longer than one week but less than three years duration. Fifteen were restored to regular sinus rhythm by means of procaine amide. In three, the auricular fibrillation was converted to auricular flutter but restoration to sinus rhythm could not be accomplished. For conversion in this group, 3 to 6 g. of the drug were usually required. There were several instances of rather severe toxicity, but the effects did not last more than 36 hours. Much nausea, diaphoresis, and prostration occurred in two subjects. Hypotension was not observed. In one patient (J. G.) whose cardiogram revealed "unstable bundle branch block" dependent upon a critical ventricular rate, the ventricular rate became rapid, about 170, after procaine amide and the cardiogram then resembled ventricular tachycardia (Vesell and Kraemer, 1951; Langendorf, 1948; and Kay, 1948). At that time the patient experienced severe malaise and weakness. There was one instance in which, following the establishment of regular sinus rhythm, a cerebral embolism occurred. Sinus rhythm was restored with quinidine in only one of the patients in whom the arrhythmia could not be abolished with procaine amide. In a second fibrillation was converted to flutter but sinus rhythm could not be established.

Group C. There were 15 patients in whom auricular fibrillation had been known to be present for three years or longer. Only three could be restored to regular sinus rhythm by use of procaine amide. Each of the three patients in whom restoration of sinus rhythm took place received 5 g. of the drug within 20 hours. Seven of those who did not respond to procaine amide were given quinidine sulphate by mouth: 0·4 g. every two hours. In none of these was restoration of sinus rhythm accomplished. In this group of patients there were two instances of untoward reactions in the form of severe gastro-intestinal symptoms; nausea, epigastric distress and a sensation of fullness in the throat.

Auricular Flutter. Regular sinus rhythm was restored in only one of seven instances of auricular flutter by means of procaine amide. In this patient, when the drug was withdrawn, auricular flutter recurred and sinus rhythm was again restored with procaine amide. The presence of auricular flutter had been recognized for six months and previous attempts at conversion with quinidine sulphate orally had failed. The flutter proved remarkably sensitive to procaine amide, responding to doses of 0·5 g. every four hours, conversion occurring when only 1·5 g. of the drug had been taken. Five of the other patients with auricular flutter were quite resistant to procaine amide. One received 12 g. of the drug within 36 hours. Two of these patients showed severe systemic and gastro-intestinal reactions to the drug. One patient, with multiple pulmonary emboli, expired suddenly while under therapy; it was believed that death was due to a pulmonary embolus and not to the drug.

Quinidine sulphate was without effect in two subjects, but converted the flutter to auricular

fibrillation in one other. An effect similar to that which has been observed with quinidine was noted in one patient with auricular flutter after he had received 1 g. of procaine amide; as the flutter rate was slowed from 216 to 188 a one-to-one ventricular response took place. Ventricular complexes at the rapid rate were of the previous supraventricular type. However, over the course of the succeeding hour, they gradually widened to 0·16 sec. without any change in the heart rate. This stimulation of ventricular tachycardia was due to the drug-induced " bundle branch block " and disappeared within two hours.

Paroxysmal Auricular Tachycardia. There were nine patients with this arrhythmia. All were successfully restored to regular sinus rhythm by means of procaine amide. Conversion occurred in all cases when between 3 and 5 g. of the drug had been taken. In four, the drug was withdrawn, the arrhythmia recurred and was again controlled by means of procaine amide. The arrhythmia in one of these patients had previously proved refractory to quinidine. There was only one instance of marked toxicity in this group.

Auricular Premature Contractions. In two of three subjects, auricular premature contractions were successfully abolished by the use of procaine amide, in dosages of 1 g. every six hours.

Nodal Tachycardia. There were four patients with nodal tachycardia. All were readily returned to sinus rhythm with procaine amide, one after receiving 3 g. of the drug, and the other two after 4 g. each. No toxic effects were noted.

Others. One patient with heart block and ventricular premature systoles was observed. This patient, with complete heart block and the pacemaker for the ventricle in the A-V node or bundle, was treated with procaine amide because of the presence of ventricular extrasystoles which were thought to be of clinical significance. She was a 68-year-old woman with arteriosclerotic heart disease and congestive heart failure, and received 2 g. of procaine amide by mouth within eight hours. A cardiogram then revealed more frequent ventricular extrasystoles, including bigeminy. A third gram of procaine amide was given. One hour later she suddenly expired. Necropsy revealed no immediate cardiac cause of death.

Maintenance

Maintenance with procaine amide is an important problem and requires further study. The number of patients in this series with adequate follow-up, after conversion to sinus rhythm, were insufficient to permit more definite conclusions. In the majority, after conversion, a maintenance dose of 0·5 g. every six hours was instituted and continued for two to four weeks. Following gradual withdrawal of the drug at that time, sinus rhythm was maintained.

In six patients requiring continuous maintenance over prolonged periods of time (one month or longer), we have noted a sensitivity to the dosage level of the drug. In one, as little as a 10 per cent reduction in dosage per day resulted in recurrence of the arrhythmia with restoration of sinus rhythm when larger doses were given. Two of these patients gradually developed tolerance to the drug. The increasing dosage level necessary for control of the arrhythmia finally could not be secured without undesirable side effects. Both of these had previously demonstrated similar behaviour with quinidine.

Discussion

The above data indicate that procaine amide, taken by mouth, may have an important effect upon arrhythmias of supraventricular origin (Garlett *et al.*, 1951; Bernstein *et al.*, 1951; and Schoffer *et al.*, 1951). A substantial number of these arrhythmias may be converted to regular sinus rhythm. Several factors have been considered in respect to the influence of procaine amide upon these arrhythmias.

Arrhythmias of recent origin, as would be expected, responded most satisfactorily to the drug. However, 10 instances in which withdrawal of the drug resulted in recurrence of the arrhythmia with subsequent restoration of sinus rhythm when the drug was reintroduced, confirm us in the belief

that in the great number of these patients procaine amide was responsible for the restoration of the normal rhythm.

Full digitalization had no significant effect upon the action of the drug. In several patients restoration of sinus rhythm was accomplished both before and after this.

The presence or absence of heart failure did not seem to influence the ability of procaine amide to abolish the arrhythmia. Three patients in frank congestive heart failure were returned to sinus rhythm with procaine amide. In two of these, the return to sinus rhythm was followed by disappearance of the congestive heart failure; the third required digitalization.

There were no cases of acute rheumatic fever in this series. Four of the patients with rheumatic heart disease were suspected of having low grade activity of the rheumatic process. In these patients, procaine amide had the following effect: the arrhythmia was abolished in one; auricular fibrillation was converted to auricular flutter in two; and in the fourth patient (J. G.), toxic effects were produced.

In this series there were arrhythmias that could not be abolished by the use of quinidine sulphate but responded well to procaine amide. The converse was also observed. In most subjects both drugs exhibited similar effects; i.e. regular sinus rhythm was re-established, auricular fibrillation was converted to auricular flutter, or no effect upon the arrhythmia was produced (Schoffer *et al.*, 1951).

Toxic effects included changes in the cardiogram. These may be most simply described by stating that all complexes of the cardiogram may show distortion under the influence of procaine amide (a more complete report on these findings is in preparation).

Toxic symptoms included epigastric distress, nausea, vomiting, choking sensations, severe malaise, marked diaphoresis, and prostration. Hypotension, which occurs frequently with intravenous administration of the drug, was not observed. However, during the period when large doses were administered, the patients were kept in bed. Therefore, possible postural effects were not observed.

There were eight patients who exhibited the above complaints to a pronounced degree. Less severe symptoms were often present. It should be noted that restoration of sinus rhythm was accomplished in only one patient by continuing procaine amide beyond the toxic effect.

There were two instance of accidents during the course of treatment. One patient sustained a cerebral embolism after auricular fibrillation was converted to regular sinus rhythm. This was the only instance of cerebral embolism in the 44 patients with auricular fibrillation and six with auricular flutter among whom there were over 30 conversions of rhythm. Anticoagulant drugs were not used. The second with auricular flutter and multiple pulmonary infarctions was receiving the drug when he suddenly expired. No statement could be made as to the cardiac rhythm just before death. Another pulmonary embolus may have occurred. Necropsy was not done.

In regard to the patient with complete heart block, we believe that procaine amide should not have been used even though extrasystoles were present. Usurpation, not escape, is the indication for the drug. The A-V node appears to be quite sensitive (Kayden *et al.*, 1951). It is possible that the node was more readily suppressed than the ectopic ventricular foci. Thus, when the A-V node is performing a vital function, such as emergency pacemaker for the heart, procaine amide should not be used.

A most interesting observation was recently reported in which the auricular arrhythmia proved to be more sensitive to procaine amide than the associated ventricular arrhythmia (Bernstein *et al.*, 1951). In two patients reported, with simultaneous dissociated paroxysmal tachycardia after intravenous procaine amide, the auricular disorder was converted to a sinus rhythm without the conversion of the ventricular.

Tachycardias of auricular and nodal origin, as well as ventricular tachycardia, are indications for the use of procaine amide. Auricular premature contractions and auricular fibrillation of recent origin respond well. Chronic auricular fibrillation or auricular flutter are difficult to abolish with procaine amide, responding in about 25 per cent of the cases.

Summary and Conclusions

Observations upon one hundred instances of arrhythmia or tachycardia of supraventricular origin occurring in 83 subjects are reported. Arrhythmias included auricular premature contractions, auricular and nodal tachycardia, auricular fibrillation and flutter. The restoration of regular sinus rhythm through the use of orally administered procaine amide has been accomplished in a significant proportion.

The type and duration of heart disease, the presence of congestive heart failure, and the influence of digitalis have all been shown to have little significant effect upon the response of the arrhythmia to procaine amide.

The type and duration of the arrhythmia is felt to be of the greatest importance in influencing the response to procaine amide. Auricular fibrillation and auricular flutter of over three years duration were resistant to the action of procaine amide while nodal rhythms were quite sensitive.

Some auricular arrhythmias that were refractory to quinidine were abolished by procaine amide. The converse was also observed.

Toxic effects of procaine amide noted in this series have included nausea, vomiting, malaise, weakness, marked diaphoresis, and profound prostration. Hypotension has not been noted. Cardiographic changes have been recorded.

It is concluded that orally administered procaine amide is of value in the control of arrhythmias and tachycardias of supraventricular origin.

We wish to express or appreciation to the members of the medical staff of the Beth Israel Hospital for their kind co-operation which made this study possible.

References

Bernstein, L. M., Pascale, L. R., Littman, A., and Foley, E. F. (1951). *Proceedings 24th Annual Meeting of American Heart Association*, p. 37, Atlantic City.
Garlett, E. L., Berry, K., and Bellet, S. (1951). *Amer. Fed. Clin. Res.*, Atlantic City.
Joseph, S. I., Helrich, M., Kayden, H. J., Orkin, L. R., and Rovenstein, E. A. (1951). *Surg. Gyn. and Obs.*, **93**, 75.
Kayden, H. J., Steele, J. M., Mark, L. C., and Brodie, B. B. (1951). *Circulation*, **4**, 13.
Kay, H. B. (1948). *Brit. Heart J.*, **10**, 177.
Kinsman, J. M., Clay, H. L., Coe, W. S., and Best, M. M. (1951). *Proc. Assoc. Amer. Physicians.* Atlantic City.
Langendorf, R. (1948). *Acta Cardiol.*, Supplement III, 13.
Mark, L. C., Berlin, I., Kayden, H. J., Rovenstine, E. A., Steele, J. A., and Brodie, B. B. (1950). *J. Pharmacol. Exper. Therap.*, **98**, 21.
Miller, H., Nathanson, M. H., and Griffith, G. C. (1951). *J. Amer. med. Assoc.*, **146**, 1004.
Schoffer, A. I., Blumenfeld, S., Pitman, R., and Dix, J. H. (1951). *Amer. Heart J.*, **42**, 115.
Stearns, N. S., and Callahan, E. J. (1951). *Program 43rd Annual Meeting Amer. Soc. Clin. Invest.*, p. 55, April.
Vesell, H., and Kraemer, L. B. (1951). *Amer. Heart J.*, **41**, 280.

PROCAINE AMIDE IN THE CONTROL OF CARDIAC ARRHYTHMIAS

BY

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Recent developments in cardiac surgery and modern methods of cardiac investigation have emphasized the need for a drug that will control the irritability of the heart, particularly ventricular arrhythmias. In clinical cardiology also a satisfactory drug for the treatment of ventricular tachycardia has still to be found, one, moreover, that can be administered parenterally with safety. The usefulness of procaine has been limited by its side effects, hypotension and excessive central nervous stimulation. The amide of procaine has not these disadvantages to the same degree, and early reports (Mark *et al.*, 1950; Newman and Clark, 1950) have emphasized its value in the control of arrhythmias. It is the purpose of this paper to report on the efficacy of procaine amide in the control both of clinical arrhythmias and of those occurring during mechanical interference with the heart, either during cardiac catheterization or during cardiac surgery.

Clinical Arrhythmias

Procaine amide* was administered to fifty-six patients, three of whom had two types of arrhythmia; five with ventricular tachycardia, eighteen with ventricular extrasystoles, eleven with supraventricular tachycardia, six with supraventricular extrasystoles, eighteen with auricular fibrillation, and one with auricular flutter. It was used both to treat current arrhythmias and to prevent recurrence. Intravenous and oral routes of administration were employed, although in order to obtain unequivocal results, the intravenous route was preferred. The dose did not exceed 1 g. intravenously or 4 g. daily by mouth. The results are shown in the table.

Ventricular Tachycardia. Five patients with ventricular tachycardia were treated by procaine amide 0·25 g. to 0·6 g. Success was achieved in four and in these the mode of reversion to sinus rhythm was studied. Three showed an abrupt cessation of the tachycardia followed by a short period during which the sinus rhythm was interrupted by frequent ventricular extrasystoles. In the fourth, sinus complexes gradually replaced the ectopic beats. The only failure was a patient with complete heart block in whom the dose was limited to 0·3 g. This was the only case of known ischæmic origin.

Ventricular Extrasystoles. Ventricular extrasystoles were also abolished by small doses of procaine amide administered intravenously. They disappeared within a few minutes of the end of the injection but reappeared forty minutes to two hours later. Therapy by the oral route was successful in seven out of thirteen instances. In three others the number of extrasystoles was reduced, but in one no effect was noticed after 2·5 g. Success was unrelated to the electrocardiographic pattern or to the ætiology. In six patients the arrhythmia was associated with ischæmic heart disease and in four with digitalis therapy; in the remainder the ætiology was uncertain.

Supraventricular Tachycardia. Four out of nine episodes of supraventricular tachycardia were terminated; one by oral administration. In three of the eight patients, the arrhythmia was apparently nodal in origin; one was suppressed for twenty minutes only and the other two were slowed

* The procaine amide (pronestyl) used in this investigation was supplied by E. R. Squibb & Sons.

TREATMENT OF ARRHYTHMIAS

Arrhythmia	Termination						Prevention		
	Cases	Episodes	Route	No.	Success	Successful dose (g)	No.	Success	Successful dose (g)
Ventricular tachycardia	5	8	I.V.	5	4	0·25–0·6	4	1	0·5 t.i.d.
			oral	3	1	0·75			
Ventricular extrasystoles	18	18	I.V.	5	5	0·2–0·5	9	4	0·5–1·0 t.i.d.
			oral	13	7	0·5–1·0			
Supraventricular tachycardia	8	9	I.V.	7	3*	0·2–0·8	6	—	
			oral	2	1	3·0 in 24 hr.			
Supraventricular extrasystoles	6	6	I.V.	3	2	0·45 & 0·5	2	—	
			oral	3	–				
Auricular fibrillation	18	19	I.V.	10	2	0·5 & 0·7	—		
			oral	9	1	2·5 in 2 hr.			
Auricular flutter	1	1	I.V.	1	—		—		
			oral	—					

* In one other patient the arrhythmia was terminated by carotid sinus pressure following the intravenous administration of 0·5 g. of procaine amide. Carotid sinus pressure beforehand had failed.

without being terminated. In one patient in whom auricular tachycardia was known to have been present for many weeks, the oral administration of 3 g. of procaine amide in twenty-four hours was followed by a Stokes-Adams attack, a period of slow nodal rhythm preceding the establishment of sinus bradycardia. It was discovered subsequently that a similar occurrence had followed treatment with large doses of quinidine.

Supraventricular Extrasystoles. Supraventricular extrasystoles were abolished in two out of six instances, on both occasions by intravenous administration. In one patient with sinus bradycardia who was showing frequent nodal escape, the administration of 0·8 g. intravenously resulted in nodal rhythm due to temporary suppression of sinus activity.

Auricular Fibrillation. Of eighteen patients with auricular fibrillation, sinus rhythm was restored in three in whom the arrhythmia had been present for less than seven days. In the remainder the auricular rate was retarded.

Auricular Flutter. In the one patient with auricular flutter the paroxysm terminated forty-five minutes after intravenous administration of procaine amide, but since by this time the peak effect on the auricular rate was past, this result is regarded as probably coincidental.

Prophylactic Treatment. In the prophylaxis against recurrence no effect was observed on any of the six patients with supraventricular tachycardia or on the two with auricular extrasystoles. Of four patients with repeated attacks of ventricular tachycardia satisfactory control was obtained in one; in another there was a reduction in the number of attacks. Ventricular extrasystoles were abolished in four out of nine patients, satisfactory control being maintained in one for five months. In two of the remainder, although some reduction was noted initially, it was not maintained.

CARDIAC CATHETERIZATION

Twenty-eight patients were studied: thirteen with mitral stenosis (six with auricular fibrillation being digitalized), eleven with congenital heart disease, and four others. Right heart catheterization

was performed under local anæsthesia after premedication with sodium amytal. Pressures were recorded with an electro-manometer, mean pressures being determined by electrical integration. The electrocardiogram, which was observed continuously, was recorded when abnormalities were noticed and when the catheter was in the right ventricle.

Initially procaine amide was given to six patients in order to determine its effect on pulmonary artery pressures. The dose varied from 0·25 g. to 0·5 g. In five (mean pressures 60, 55, 36, 34, and 7 mm. Hg), there was a fall and in one (mean pressure 27 mm.) a rise, but in none did the variation exceed 5 mm. In one the pulmonary artery pressure recorded for twelve minutes before administration showed a variation of 4 mm.

Ventricular extrasystoles occur most frequently when the tip of the catheter is at the tricuspid area or in the right ventricular outflow tract. When extrasystoles occurred at this stage in three selected patients premedicated with quinidine 3 grains, the catheter was withdrawn and procaine amide, 0·5 g. to 0·75 g., administered intravenously. After five minutes the procedure was repeated. In one the drug had no effect; in another the number of ventricular extrasystoles was halved and in the third they disappeared, but reappeared spontaneously twenty-five minutes later, after the catheter had been withdrawn.

Procaine amide was then given intravenously to ten patients as soon as the catheter had been inserted. The dose varied from 0·25 g. to 0·5 g. Ventricular extrasystoles were observed in eight; four had paroxysms persisting for seven or more beats, one as long as nineteen beats.

Finally, procaine amide was administered orally to fifteen patients half an hour before catheterization in a dose varying from 0·5 g. to 1 g. Ventricular extrasystoles were observed in twelve, four having paroxysms which persisted for seven or more beats, the longest being thirteen (Fig. 1).

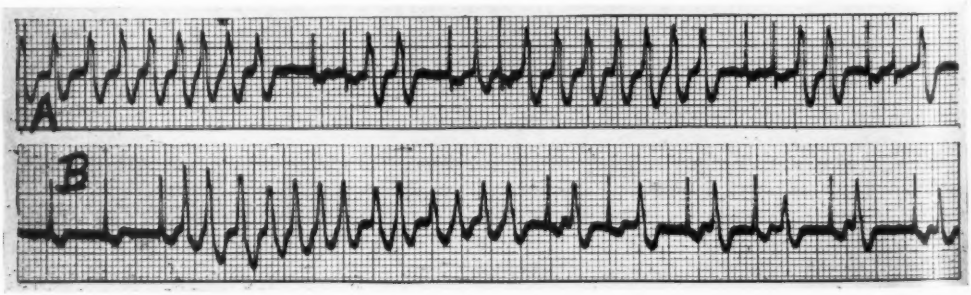

FIG. 1.—Ventricular arrhythmias during cardiac catheterization. (A) 25 minutes after procaine amide 0·5 g. intravenously. (B) 60 minutes after procaine amide 1·0 g. orally.

CARDIAC SURGERY

Patients undergoing direct heart operations were selected for study. All were anæsthetized with the same technique: omnopon and scopolamine premedication; induction with thiopentone and curare, and maintenance with nitrous oxide and oxygen, using a controlled respiration technique. Further doses of thiopentone and curare were administered as required. Prior to the opening of the pericardium 2 to 5 ml. of 0·25 per cent amethocaine was instilled into it and the heart itself was infiltrated with 1 per cent procaine around the area of incision. The electrocardiogram was observed continuously and was recorded when abnormalities were noticed and during the endocardial manœuvres.

The effect of intravenous procaine amide on the arrhythmias that occur during manipulation of the heart was studied in twenty-four patients: sixteen with mitral stenosis and eight with cyanotic congenital heart disease. The dose varied from 0·1 g. to 0·5 g. according to body weight. Those with mitral stenosis were digitalized at the time of operation, with the exception of four who received

quinidine, 5 to 10 grains, preoperatively. Six patients with cyanotic congenital heart disease also received quinidine, 1 to 5 grains, the other two being given oral procaine amide, 0·25 g. and 0·5 g.

Following the administration of procaine amide, ventricular ectopic beats were observed in nine of the patients with mitral stenosis. These varied from a few while the heart was being manipulated to paroxysms of ventricular tachycardia necessitating the abandonment of the operative manœuvre. Ventricular ectopic beats were also observed in seven of the eight patients with cyanotic congenital heart disease.

Toxic Effects

Apart from gastro-intestinal disturbances and hypotension, no important toxic effects were observed throughout this investigation, nor were any significant changes found in the electrocardiogram. Nausea and vomiting occurred in a proportion of the twenty-four patients who received prolonged oral administration of procaine amide and in six these symptoms were severe enough to necessitate withdrawal of the drug although in two the dose did not exceed 0·5 g. t.i.d. In two others nausea and vomiting occurred at the outset, but disappeared spontaneously despite continued therapy.

A fall of blood pressure was frequently observed following intravenous administration and a special study of this was made on thirty occasions when the drug was given by this route. In twenty-two instances the dose did not exceed 0·7 g.; in nine there was no fall of blood pressure, in four a fall of up to 10 per cent and in nine a fall of 10 to 25 per cent. Eight patients received 0·75 g. to 1 g.; a fall of between 10 and 25 per cent occurred in three and 30 to 40 per cent in five. There was no apparent correlation between speed of administration and hypotensive effect.

Discussion

An analysis of four papers (Kayden *et al.*, 1951; Miller *et al.*, 1951; Berry *et al.*, 1951; Kinsman *et al.*, 1951) reporting 279 cases of clinical arrhythmia treated with procaine amide shows that ventricular tachycardia was terminated in 69 per cent, ventricular extrasystoles in 91 per cent, supraventricular tachycardia in 68 per cent, auricular fibrillation in 7 per cent, and auricular flutter in 5 per cent. The treatment of auricular fibrillation was successful only if it was of recent origin. The present investigation supports this analysis.

Corresponding figures relating to the prophylaxis of arrhythmias are not available. In the present series procaine amide was uniformly unsuccessful in preventing supraventricular arrhythmias and only succeeded in a minority of ventricular arrhythmias. In some patients, however, ventricular extrasystoles were suppressed for periods of one to five months. The failure of oral procaine amide to achieve long-term control may be related to its rate of removal from the blood-stream which is approximately twice as rapid as that of quinidine (Mark *et al.*, 1951). In a significant proportion of patients, the maintenance of a therapeutic blood level was prevented by vomiting.

The fact that procaine amide slows the auricular rate in auricular fibrillation is in agreement with the view that its action resembles that of quinidine (Newman and Clark, 1951; Wedd *et al.*, 1951), and implies a need for caution in the presence of conduction defects. In the present investigation the administration of the drug to two patients with sino-auricular block led to auricular standstill. It is interesting that two patients whose attacks of ventricular tachycardia were terminated by procaine amide had failed repeatedly to respond to quinidine in full dosage. On the other hand, quinidine was effective in two patients with paroxysmal supraventricular tachycardia and one with multiple auricular extrasystoles in which procaine amide failed.

Summary and Conclusions

This investigation, based on the treatment of 56 patients with clinical arrhythmias, 28 patients undergoing cardiac catheterization, and 24 patients submitted to cardiac surgery, has confirmed the

value of procaine amide in the termination of paroxysmal tachycardia. It has also confirmed the safety of the intravenous route of administration provided the hypotensive effect of large doses is borne in mind.

Procaine amide is of limited value in the prophylaxis of clinical arrhythmias and of no value in the prevention of the arrhythmias arising during mechanical interference with the heart.

We are grateful to the Physicians of the National Heart Hospital and especially Dr. Paul Wood for their help and to Mr. J. Brabrook-Norman for his technical assistance in this investigation.

References

Berry, K., Garlett, E. L., Bellet, S., and Gefter, W. I. (1951). *Amer. J. Med.*, **11**, 431.
Kayden, H. J., Steele, J. M., Mark, L. C., and Brodie, B. B. (1951). *Circulation*, **4**, 13.
Kinsman, J. M., Hansen, W. R., and McClendon, R. L. (1951). *Amer. J. med. Sci.*, **222**, 365.
Mark, L. C., Berlin, I., Kayden, H. J., Rovenstine, E. A., Steel, J. M., and Brodie, B. B. (1950). *J. Pharmacol.*, **98**, 21.
——, Kayden, H. J., Steele, J. M., Cooper, J. R., Berlin, J., Rovenstine, E. A., and Brodie, B. B. (1951). *J. Pharmacol.*, **102**, 5.
Miller, H., Nathanson, M. H., and Griffith, G. C. (1951). *J. Amer. med. Ass.*, **146**, 1004.
Newman, P. J., and Clark, B. B. (1950). *Fed. Proc.*, **9**, 304.
——, ——, (1951). *Fed. Proc.*, **10**, 326.
Wedd, A. M., Blair, H. A., and Warner, R. S. (1951). *Amer. Heart J.*, **42**, 399.

CONGENITAL HEART DISEASE IN ONE OF UNIOVULAR TWINS

BY

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Many cases have been reported of congenital heart disease occurring in both of uniovular twins. With the exception of dextrocardia occurring as part of situs inversus (Debreuil-Chambardel, 1927), no cases have been reported in which the lesion has been confined to one of such twins. As uniovular twins are usually similar in size as well as appearance (Stocks, 1930) the occurrence of a defect in one would be a valuable natural experiment yielding information regarding the effects of the lesion upon development. It would also throw further light upon the hereditary factors governing the transmission of the defect.

A lesion causing growth impairment in one of monozygotic twins is also rare. Milne (1951), reporting two pairs of twins in whom growth disparity was due to renal dwarfism, noted four other reported cases. Two were due to skeletal deformities (Siemens, 1927; Lehmann, 1937) and two were due to endocrine dysfunction (Komai and Fukuoka, 1934; Lewis, 1936). A further case, due to congenital syphilis, has been reported by Penrose (1937).

Two cases of congenital heart disease occurring in only one of a pair of twins believed to be uniovular are reported in this paper. In one the lesion was a patent ductus arteriosus and observations have been made on the development of this child and of her twin over a period of 2½ years after successful ligation of the ductus. In the other the lesion was thought to be isolated pulmonary stenosis.

Case Reports

Case 1. The patient was a seven-year-old girl, one of a family of nine, and had a twin sister. Both weighed 6¼ lb. at birth. Pregnancy and confinement were uneventful. When two years old she was admitted to hospital on account of a respiratory infection and a heart murmur was heard. She had otherwise enjoyed good health but had always been smaller and less active than her twin.

On examination she was a slender girl. There was a systolic-diastolic murmur loudest in the second left interspace characteristic of a patent ductus arteriosus. The blood pressure was 125/60 mm. A teleradiogram showed some prominence of the pulmonary artery, a rather small aorta, and a cardiothoracic ratio of 0·62. The electrocardiogram was within normal limits.

The ductus was ligated by Mr. Graham Bryce, and convalescence was uneventful. When last seen two and a half years later her mother stated that she was more active than her twin sister.

Comparison of the twin. The twin sister was a normal healthy girl. A radiological examination was not made at the time of the first visit. Fig. 1 shows comparative teleradiograms 14 months after operation. The heart of the normal child is still smaller, though as usual the heart of the sister had diminished in size after the closure of the ductus.

Apart from the difference in physique, the children were very similar. The shape of the head and ears, the colour and distribution of the hair, the colour of the eyes, and the dental patterns were alike. The finger prints were reported on as follows: "The ridge characteristics do not fall on the same sequence and therefore the prints are not identical, but there is a marked general similarity." Finally, blood tests with twelve different sera revealed no difference. There seems to be little doubt, therefore, that the twins were uniovular (Newman, 1940).

TABLE I

COMPARATIVE MEASUREMENTS OF THE TWO REPORTED CASES AND THE TWIN SISTERS

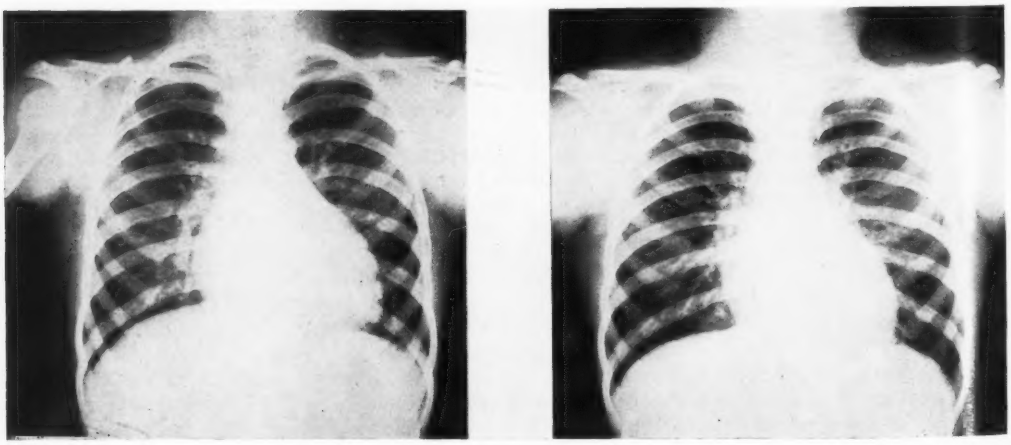
	Height in inches	Weight in pounds
Case with patent ductus arteriosus	45·2	43
Normal twin	47·2	48
Case 30 months after ligation	50·5	52·5
Normal twin	51·5	56·5
Case 2 with isolated pulmonary stenosis	61·1	94·3
Normal twin	61·1	94 8

Case 2. The patient, a fourteen-year-old girl, had a twin sister. They were born 6 weeks prematurely but pregnancy and confinement were otherwise uneventful. Both weighed 3½ lb. at birth. A heart murmur was discovered when she was 18 weeks old but subsequent development was normal and equalled that of her sister. She was able to hold her own with other children and her sister at games and gymnastics.

On examination she was a well developed girl. The cardiac impulse was diffuse and there was a thrill palpable in the second left interspace. There was a loud systolic murmur maximal in the same area and the second sound was poorly heard to the left of the sternum. The blood pressure was 130/70. A teleradiogram (Fig. 2A) showed enlargement of the pulmonary trunk and the right ventricle. An electrocardiogram (Fig. 3) showed changes diagnostic of right ventricular preponderance. The lesion was considered to be isolated pulmonary stenosis.

Comparison of the twin. The twin sister was a normal healthy girl. There was a soft systolic murmur in the pulmonary area, but otherwise the cardiovascular system was normal. The blood pressure was 135/75. A teleradiogram (Fig. 2B) revealed a normal cardiac contour. The electrocardiogram was within normal limits.

It was almost impossible to distinguish the one child from the other, all comparable details being very similar. The finger prints were reported on as follows: "There is a marked similarity in the patterns of comparable fingers, but the prints are not identical." Blood tests showed no serological

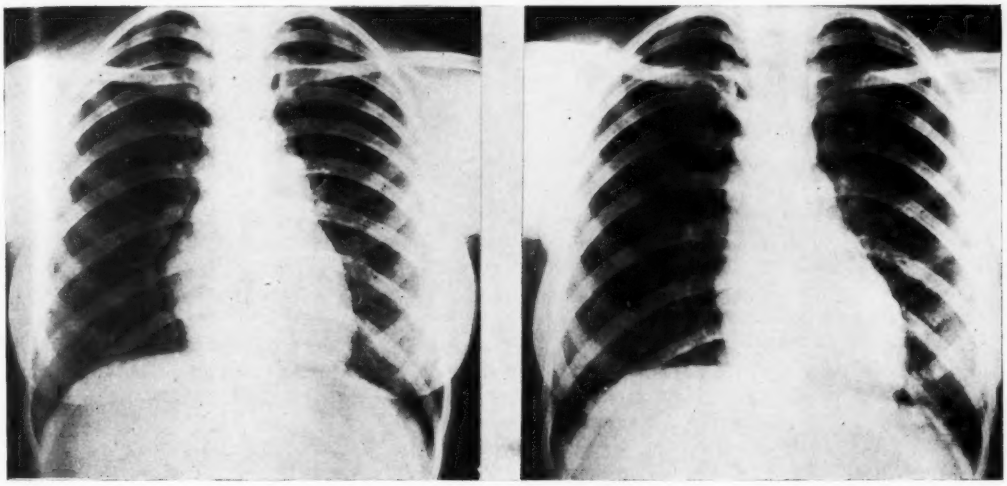


A B

FIG. 1.—Comparative teleradiograms of Case 1 (A) and her twin sister (B), fourteen months after closure of the ductus. The heart of the affected child is still larger than her normal twin.

differences. By the criteria of Newman (1940), therefore, it is highly probable that the twins were uniovular.

The measurements of the two cases and the twin sisters are compared in Table I.



A B

FIG. 2.—Comparative teleradiograms of Case 2 (isolated pulmonary stenosis) (A) and her twin sister (B). In the former there is enlargement of the pulmonary artery and the right ventricle.

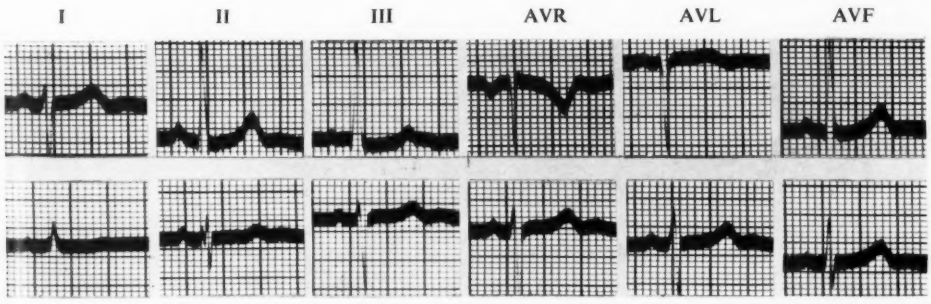


FIG. 3.—The electrocardiogram from Case 2. There is abnormal right axis deviation. The R wave over the right præcordium and the large S wave over the left præcordium (V2-V4) indicate right ventricular enlargement.

DISCUSSION

The ætiological factors concerned in congenital heart disease are divided into genetic and environmental. The environmental factors are generally regarded as virus infections, syphilis, avitaminosis, irradiation, or skeletal deformities. Campbell (1949), reporting three hundred cases of congenital heart disease, concluded that the causes were mainly genetic, a conclusion supported by the number of families reported with more than one member exhibiting congenital defects

(Walker and Ellis, 1940/41; Gilchrist, 1945; Taussig, 1947; Campbell, 1949). Campbell (1949) has stated that some 7 per cent of patients have relatives with congenital defects. Murphy (1940), reviewing the evidence, concluded that malformations, as they occurred in random samples of the population, were due to inherited factors in the germ plasm prior to fertilization.

If these conclusions are correct the same defect must be expected to occur in both of monozygotic twins for they must be genotypically identical. Such cases have been reported many times. An exception to this may be dextrocardia occurring as part of situs inversus, for Newman (1928) has suggested that if twinning occurs at the stage of late gastrulation when differentiation of the right and left sides has already taken place, reversed symmetry may occur. This may account for the case reported by Debreuil-Chambardel (1927).

Other explanations must be sought, therefore, to explain the cases reported in this paper. Firstly, there may be an abnormality of intra-uterine environment which has affected the development of one twin only. Such an explanation cannot account for the undoubted hereditary factor in congenital heart disease and would also seem to be unlikely to influence closure of the ductus, an event that occurs after birth. There was nothing to suggest any of the usual environmental factors in either of the reported cases. Secondly, the gene carrying the defect may be of very low penetration requiring some coincidental environmental change to permit expression. Gates (1946) has pointed out that this may happen, thereby causing differences in monozygotic twins.

This latter theory provides the most acceptable explanation of the known hereditary factors and of these two reported cases. The factors that normally cause closure of the ductus arteriosus are imperfectly known, although Klotz (1907) has stressed the role of pressure changes in the ductus at birth and Kennedy and Clark (1942) have clearly shown the importance of the first inspirations of oxygen: the interplay of these factors must vary considerably from case to case and a certain combination may be necessary to bring about expression of the gene. Pulmonary stenosis differs in that it develops in utero. It is difficult to understand how changes in intra-uterine environment may effect development of only one of two monozygotic embryos, yet the well documented case reported by Penrose (1937) in which congenital syphilitic stigmata were confined to one of such twins, provides good reason for believing that it may do so.

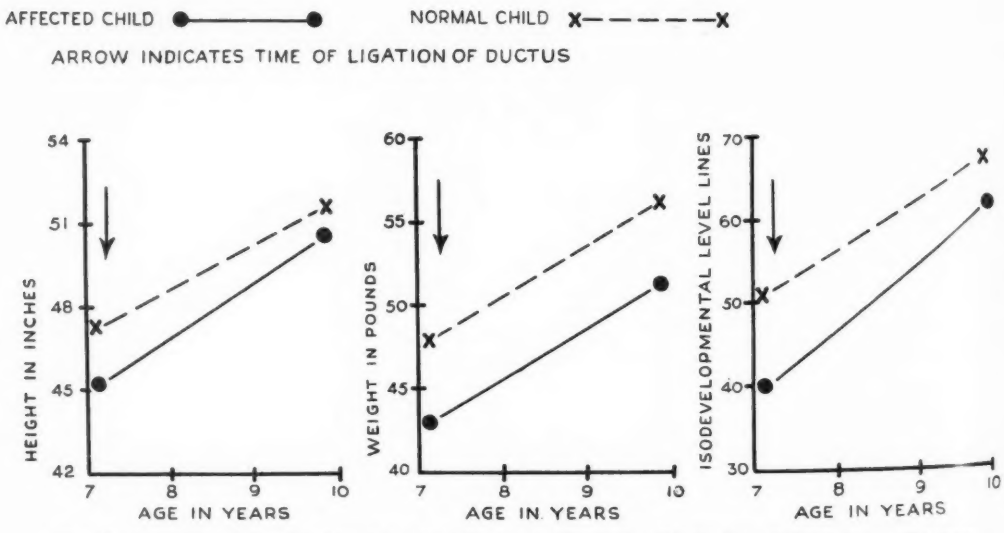


FIG. 4.—Progress of Case 1 and her twin sister during the 30 months after ligation of the ductus. The three graphs show the gains in height, in weight, and in the isodevelopmental level lines of Wetzel.

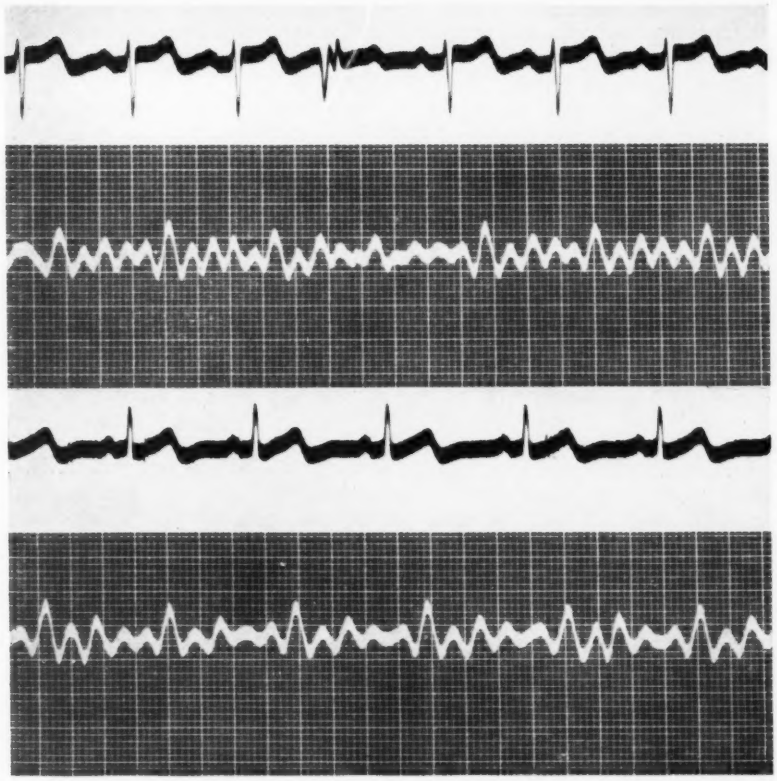


FIG. 5.—Ballistocardiographs from Case 2 with pulmonary stenosis (A) and her twin sister (B). The simultaneous electrocardiograph is lead I in each case.

The biometric studies of Stocks (1930) led him to conclude that a difference in height greater than the appropriate standard deviation was rarely, if ever, found in monozygotic twins. In Case 1, in which the lesion was a patent ductus, the difference in height before operation was 2 inches and the standard deviation 1·6 inches. With the same genetic and, after birth, the same environmental factors in both children, it is reasonable to ascribe the difference in height to the patent ductus. The slender build and underdevelopment of children with this defect has been previously noted by Porter (1947) although not by Benn (1947). Lessening of the systemic flow, due to part being lost into the pulmonary circuit, is generally regarded as being the cause of the impaired development. The volume of the shunt in the reported case was not known, but the heart size suggests that it was of at least moderate dimensions. The pulmonary vasculature, however, was normal.

Following the closure of the ductus the affected child developed more rapidly than the normal child. In Fig. 4 the progress of the children is shown diagrammatically. The three graphs show the gains in height and weight and their progress on the physical fitness grid of Wetzel (1944). In this system, height is plotted against weight and the resultant measured by what are termed " isodevelopmental level lines." These level lines are then plotted against age. The method therefore takes into account both height, weight, and age in assessing development. It will be seen that the affected child advanced 22 level lines, while the normal child advanced only 17½ during the period of observation. The graphs for height and weight show that this advance was mainly due to a gain in relative

height without a corresponding gain in relative weight. This is significant, for Verschuer (1928) found that, in monozygotic twins, height was the anthropomorphic measurement least affected by environment. Gilchrist (1945) commented on the increase in growth that may follow successful operation.

Although growth may be improved, or at least rendered normal after operation, our observations suggest that lost ground is made up slowly and possibly not completely. From this point of view, it therefore seems desirable to ligate the ductus as early as possible and especially before the period of rapid growth which is ushered in with the second decade.

In Case 2, in which the lesion was though to be isolated pulmonary stenosis, the physique of both twins was almost identical and normal for their age. Retardation in these cases can only be due to a diminished cardiac output. The good exercise tolerance in this patient must indicate that the output was adequate under almost all conditions. Ballisto-cardiographic studies of both twins suggested that this assumption was correct.* The calculated stroke volume of the affected twin was 41 ml. and that of the normal twin 48 ml. The cardiac outputs were identical. Apart from the difference in size, the form of the records were very similar (Fig. 5).

Summary

Two cases of congenital heart disease confined to one of uniovular twins are reported. In one the lesion was a patent ductus arteriosus and in the other isolated pulmonary stenosis.

Development was impaired in the case of patent ductus arteriosus, but not in the case of isolated pulmonary stenosis. Following closure of the ductus, development improved, especially in height, but two and a half years after operation there was still a difference in the physique of the twins.

The genetics of congenital heart disease is briefly reviewed. It is suggested that, in the reported cases, the gene was of low penetration necessitating a coincidental change in environment to permit expression.

I wish to thank Professor Crighton Bramwell for his help and advice; Dr. F. Stratton for his kindness in performing the serological tests; and the Chief Constable of Manchester and the Manchester City Police for taking and reporting upon the finger prints.

References

Benn, J. (1947). *Brit. Heart J.*, **9**, 283.
Campbell, M. (1949). *Quart. J. Med.*, **18**, 379.
Debreuil-Chambardel (1927). *Presse Med.*, Paris, **35**, 1157.
Gates, R. G. (1946). *Human Genetics*. New York.
Gilchrist, A. R. (1945). *Brit. Heart J.*, **7**, 1.
Kennedy, J. A., and Clark, S. L. (1942). *Amer. J. Physiol.*, **136**, 140.
Klotz, O. (1907). *Tr. Ass. Amer. Physicians*, **22**, 213.
Komai, T., and Fukuoka, G. (1934). *J. Hered.*, **25**, 423.
Lehmann, W. (1937). *Z. Konstlehre*, **20**, 237.
Lewis, A. (1936). *Ann. Eugenics*, **7**, 58.
Milne, M. D. (1951). *Lancet*, **1**, 204.
Murphy, D. P. (1940). *Congenital Malformations*. University of Pennsylvania Press.
Newman, H. H. (1928). *Biol. Bull.*, **55**, 298.
—— (1940). *Multiple Human Births*. New York.
Penrose, L. S. (1937). *Lancet*, **1**, 322.
Porter, W. B. (1947). *Amer. J. med. Sci.*, **213**, 178.
Siemens, H. W. (1927). *J. Hered.*, **18**, 201.
Starr, I. (1947). *Amer. J. med. Sci.*, **214**, 233.
——, Rawson, A. J., Schroeder, H. A., and Joseph, N. R. (1939). *Amer. J. Physiol.*, **127**, 1.
Stocks, P. (1930). *Ann. Eugenics*, **4**, 49.
Taussig, H. B. (1947). *Congenital Malformations of the Heart*. New York.
von Verschuer, O. (1928). *Zeits. Abst. Vererb. Suppt.*, **11**, 1508.
Walker, G. C., and Eillis, L. B. (1940–41). *Proc. New Eng. Heart Ass.*, pp. 26–27.
Wetzel, N. C. (1944). *Growth in Medical Physics*. Chicago.

* In these investigations an undamped ballistocardiograph was used of the type described by Starr *et al.* (1939). The cardiac output was calculated by means of the formula devised by Starr (1947)

$$\text{Stroke volume} = \sqrt{K2\int Idt + \int Jdt}\sqrt{c}$$

where $\int Idt$ and $\int Jdt$ are the areas in millimetre-seconds of the I and J waves respectively, c = the length of the cardiac cycle, and K is a constant.

THE SIGNIFICANCE OF THE DIRECTION OF THE P WAVE IN DEXTROCARDIA AND ISOLATED LÆVOCARDIA

BY

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The electrocardiogram of dextrocardia with situs inversus is well known and is often quoted as one of the rare examples where a diagnosis can be made on the electrocardiogram alone. Taussig (1947), Wood (1950), Brown (1950), and White (1951) all accept this orthodox view, though Brown adds that the P wave may sometimes be upright in lead I: he quotes the case of Beaujeu and Bège (1937) who said that their case was the second example they had seen of a positive PI in dextrocardia with complete situs inversus. It is generally taught that except for the association with bronchiectasis and sinusitis, there is no disadvantage in having dextrocardia with situs inversus and that the heart is normal in every other way being a mirror image of the normal.

Wood (1950) says that mirror-image dextrocardia is almost invariably associated with complete transposition of the viscera. White (1951) says that in mirror-image dextrocardia, whether the abdominal viscera are transposed or not, lead I of the electrocardiogram is completely inverted. Without full investigation one does not as a rule know if a heart on the right is a mirror image or not, and the general problem is, therefore, better stated in simpler terms.

If the heart and the abdominal viscera are all transposed and the patient is acyanotic, *generally* the heart is normal and is, in fact, a mirror image of the normal. But at any large clinic for congenital heart disease there are several with other congenital malformations added to the dextrocardia and transposition of the viscera. Taussig (1947) says that her experience includes many such cases in which the other congenital malformations have produced cyanosis; and with this we are in complete agreement. Here, presumably, the heart is not a mirror image of the normal or additional defects are added to a mirror-image dextrocardia, for the presence of complete situs inversus cannot prevent a patient having Fallot's tetralogy any more than a normally placed heart can: indeed, it may make it more likely.

Isolated Dextrocardia. When, on the other hand, the heart is on the right without transposition of the abdominal viscera (isolated dextrocardia) there are *generally* other congenital malformations of the heart. Röesler (1930) maintained that this was always so, and Lichtman (1931) among 161 reported cases found only three in which there was no associated congenital malformation. Here again, the heart is presumably not a mirror image of the normal, but as suggested by White (1951) there may be some cases where the heart is a mirror image and the electrocardiogram may then show the classical picture of dextrocardia with situs inversus.

There is much less general agreement about the electrocardiogram of isolated dextrocardia. Brown divides these cases into two groups: in the first, cavities are inverted and " the electrocardiogram may or may not show the alterations characteristic of dextrocardia of the mirror-image type: the uncomplicated type presents the classical picture." In his second group the heart cavities are not inverted (dextroversio cordis), and " in cases where an electrocardiogram has been done there was no change in lead I."

Several authors in reporting single cases of isolated dextrocardia have noted the P wave is not inverted in all these cases. For example, Ruskin *et al.* (1943) reported a case of isolated

dextrocardia, a woman, aged 55, who had borne seven children. The T wave was inverted in leads I and II but the P wave was not, and they thought the electrocardiogram was typical of isolated dextrocardia. Angiocardiograms showed that there was a left-sided superior vena cava which entered the venous atrium on the right.

Isolated Lævocardia. Still less has been written about the electrocardiogram of lævocardia with transposition of the abdominal viscera. Some authors in reporting single cases of this type have noted that the P wave in lead I was inverted in some but not in all cases, although the heart was on the left.

Forgacs (1947) reported two cases: in one where an electrocardiogram was available PI was upright but PII and PIII were fairly sharply inverted. Thomson (1950) reported two cases: in one PI was upright, PII biphasic, and PIII inverted, but in the other the picture was " highly suggestive of a true dextrocardia," PI being deeply inverted and PIII upright. He said that he had found very few electrocardiographic records of this syndrome and that those published showed no uniform pattern. He referred to the case of Grieshaber (1936) and to a more doubtful one of Shaw and Blake (1924) as showing " inverted electrocardiograms ": but we think the latter is really a case of dextrocardia with the heart rather centrally placed.

Donzelot *et al.* (1949–50) also reported two cases. In both the P wave was upright in lead I, though in one it was inverted in leads II and III: in both the venous atrium was in its normal position on the right. Each had a ventricular septal defect with an over-riding aorta and one had severe pulmonary stenosis.

Young and Griswold (1951) in a valuable paper have reported their findings in 8 cases of isolated lævocardia but do not mention the direction of the P wave in this group of cases.

It is clear from these statements that there is general agreement about the inversion of P and the other waves in lead I in dextrocardia with complete situs inversus, but much less agreement about the usual electrocardiographic pattern of isolated dextrocardia without transposition of the abdominal viscera or of isolated lævocardia with transposition of the abdominal viscera. The large number of patients with congenital heart disease whom we have seen in the last few years (1947–51) have given us a chance to examine these questions more thoroughly. Among 670 cyanotic patients there were 31 with dextrocardia (usually isolated) or isolated lævocardia, and among 454 acyanotic patients there were 5 with dextrocardia or isolated lævocardia. We have added 4 others seen since, making 40 cases in all.

Findings in our 40 Cases

Changes of pacemaker with differently shaped P waves and different P–R intervals are common in congenital heart disease and these cases are no exception. These give rise to no difficulty if it is clear which is the normal sinus rhythm. As will be seen from the notes to Tables I and II, however, this is not always clear and there were cases where from time to time the P wave had a different form and direction. When there was any doubt we have taken the form that seemed most usual and have added a footnote about the changes.

Dextrocardia with Transposed Visera. There were 11 such cases. Other congenital malformations of the heart were absent in 2 patients in whom the dextrocardia was a chance finding, but were present in the other 9 of whom 2 were acyanotic and 7 were cyanotic. Two at least of these last had some lesion similar to Fallot's tetralogy as they benefitted greatly by a subclavian-pulmonary anastomosis. None of these 11 patients have died.

As would be expected, PI was inverted in 9 of these 11 with complete situs inversus, but in 2 PI was upright (Cases O347 and P086). One of the latter was investigated by angiocardiography and was certainly not a mirror-image dextrocardia, the right superior vena cava and atrium being almost in the position that is normal when the heart is on the left.

Isolated Dextrocardia. There were 15 cases with the heart on the right but with the abdominal viscera normally placed. All had other congenital malformations of the heart, 13 being cyanotic and 2 acyanotic.

Three have died. Of these, one (Case P165) had a single atrium, a single A-V valve, two ventricles, and transposition of the aorta and pulmonary trunk; one (Case P077) had pulmonary stenosis and transposition of the aorta and pulmonary trunk; and the third (Case H142) had a large atrial septal defect, a single ventricle, and pulmonary valvular stenosis (Campbell, Reynolds, and Trounce, 1953). The last was the only patient of this group in whom a subclavian-pulmonary anastomosis was attempted.

Twelve of these 15 had an upright PI so that generally the picture differs from that of dextrocardia with transposed abdominal viscera (Table I). Only 3 of the 15 had PI inversion; possibly the three exceptions had mirror-image dextrocardia without transposed abdominal viscera which is unusual.

TABLE I

THE P WAVE IN PATIENTS WITH HEART AND/OR VISCERA TRANSPOSED

	PI and PII upright	PI inverted	PII and PIII inverted	Total
Situs inversus totalis	2	9[1, 2]	0	11
Isolated dextrocardia	12[3, 4, 5]	3[6]	0	15
Isolated lævocardia	4	6[7]	4	14

1. PI was generally inverted with a P–R interval of 0·17 but sometimes upright with a P–R interval of 0·12 sec. in Case O646.
2. PI was sometimes inverted but sometimes upright with PII and PIII inverted in Case O392.
3. PI was almost flat in Case O784.
4. PI was sometimes upright but sometimes inverted with inversion of PII and PIII as well, without any change in the P–R interval in Case O237.
5. PI was triphasic, at first upright, then downwards and then again upright in Case P165.
6. PII and PIII were also inverted in Case O854.
7. PI was biphasic, though the inversion came first and was deeper, in Case P105; and PI was generally inverted but sometimes upright with PII and PIII inverted, and often with shorter P–R interval in Case O556.

Isolated Lævocardia. Although fewer cases have been reported, this seems to be about as common as isolated dextrocardia. In our series there were 14 cases with the heart on the left but with the abdominal viscera completely or mainly transposed. All had other congenital malformations of the heart, 12 being cyanotic and 2 acyanotic, almost exactly the same figures as for isolated dextrocardia.

Four have died but one had no necropsy. One (Case O136) had a bilocular heart and has been fully reported (Campbell, Gardner, and Reynolds, 1952): one (Case P130) had mitral atresia, a single ventricle, and severe pulmonary valvular stenosis (Campbell, Reynolds, and Trounce, 1953): and one (Case O405) had a ventricular septal defect, partial transposition of the aorta and pulmonary trunk, and infundibular and pulmonary valvular stenosis. In Case P130 transposition of the abdominal viscera was not quite complete.

In this group with isolated lævocardia, the direction of the P wave is less consistent than in those with either type of dextrocardia, i.e. with the abdominal viscera transposed or in their normal position. It was inverted in 6 of the 14, but upright in the other 8, though PII and PIII were inverted in 4 of these 8 (Table I and Fig 1). The anatomical significance of an upright PI with inversion of PII and PIII is not yet known, but we put forward the following hypothesis. Where the abdominal viscera are transposed, the sinu-atrial node might be expected to develop in the primitive atrium on the side opposite to the normal, i.e. below the left horn of the sinus venosus. One might now expect a superior vena cava and venous atrium to be formed on the left. If, however, the further development is reversed and results in a superior vena cava and venous atrium on the right, the sinu-atrial node, by remaining in relation to the left horn of the sinus venosus, comes to lie adjacent to the coronary sinus. Hence, the pacemaker lies in the lower part of the

right atrium with consequent inversion of PII and III. If this hypothesis is correct it may mean that the right-sided venous atrium in these cases is embryologically a left one though at an early stage its development is reversed.*

The relevant anatomy is known in one only (Case O136) and here bilateral superior venæ cavæ were present and entered a common atrium, the right directly but the left through the coronary sinus: this suggests that the venous half of the atrium was in its normal position.

Similarly, in cases with inversion of the P waves in all the standard leads the sinu-atrial node may be lying in relation to the coronary sinus entering a left-sided venous atrium.

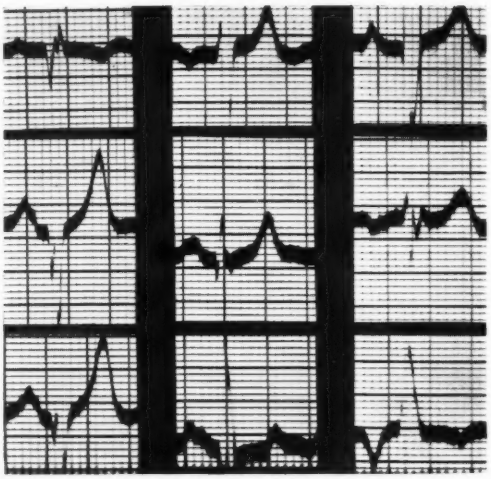

FIG. 1.—(A) The usual electrocardiogram from isolated dextrocardia, showing an upright P wave and a Q wave in lead I. (B) The common form of the electrocardiogram from isolated lævocardia showing an inverted P wave but no Q wave in lead I. (C) The less common form of the electrocardiogram of isolated lævocardia showing an inverted P wave in leads II and III.

The Relationship of the Direction of the P Wave to the Side of the Superior Vena Cava and the Venous Atrium

The direction of the P wave is, therefore, related to the position of the abdominal viscera more closely than to the position of the heart, though not constantly to either. There is, however, a constant relationship between the direction of PI and the side of the venous atrium in these cases, as shown by the superior vena cava, as far as this is known at present. In all 9 with this vessel in its normal position on the right, regardless of the side of the heart itself, PI was upright; while in all 7 with this vessel on the left, PI was inverted.

Bilateral superior venæ cavæ were present in 5 other cases; in 3 the side of the venous atrium was known and was on the right, and PI was upright in all three, PII and III being inverted in one of them (Table II).

Apart from these cases of dextrocardia and lævocardia, we have seen many examples of a persistent left superior vena cava, with both superior venæ cavæ present. In all of these the left superior vena cava reaches the right atrium through the coronary sinus, so that there is no change in the position of the venous atrium or in the pattern of the electrocardiogram.

*We have recently examined the only available heart (Case O136) and have failed to find any direct support for this hypothesis, but the heart had been preserved for two years before any sections were taken.

TABLE II

THE RELATIONSHIP OF UPRIGHT AND INVERTED P WAVES TO THE POSITION OF THE SUPERIOR VENA CAVA AND OF THE AORTA

	PI and II upright	PI inverted	PII and III inverted	Total
S.V.C. on right	9[4]	0	0	9
S.V.C. on left	0	7[2, 7]	0	7
S.V.C. on R. and L.	2*	2	1*	5
Left-sided aorta	11	4[6]	2	17
Right-sided aorta	6	13[1, 2, 7]	2	21

* These all had the venous atrium on the right.
For other footnotes see Table I.

This close relationship between the direction of PI and the side of the superior vena cava is not surprising since the P wave originates in the sinu-atrial node which lies close to the opening of the superior vena cava into the venous atrium. It is perhaps not widely recognized that the superior vena cava, venous atrium, and aortic arch are usually not transposed in an isolated dextrocardia, but are frequently transposed in an isolated lævocardia (Table III). It appears that the direction of PI will indicate whether this is so or not in any particular case.

TABLE III

THE SIDE OF THE SUPERIOR VENA CAVA AND OF THE AORTA IN PATIENTS WITH THE HEART AND/OR VISCERA TRANSPOSED

	Side of S.V.C.				Side of Aorta			Total
	R.	L.	R. & L.	Not known	L.	R.	Not known	
Situs inversus totalis	2	2	2	5	2	9	0	11
Isolated dextrocardia . .	6	1	1	7	11	2	2	15
Isolated lævocardia	1	4	2	7	4	10	0	14
Total	9	7	5	19	17	21	2	40

The Side of the Aortic Arch

Since the superior vena cava and the arch of the aorta are usually on opposite sides there is also some relationship, though a less close one, between the direction of PI and the side of the aortic arch. As it is easier to find the side of the aortic arch than of the superior vena cava or the venous atrium, this is worth considering.

In 13 of the 17 cases with a left-sided aortic arch PI was upright, while in 13 of the 21 cases with a right-sided aortic arch PI was inverted (Table II). In the 4 cases where the arch of the aorta and the superior vena cava with the venous atrium were known to be on the same side, PI had the form to be expected from the side of the superior vena cava.

Taussig (1947) says that in cases of dextrocardia (presumably with situs inversus) it is important to remember that a right-sided aortic arch is normal, but that a left-sided aortic arch is relatively common in cases of dextrocardia combined with persistent cyanosis and that this is true whether there is complete situs inversus or not. The last part of the remark is only true because in most of the cyanotic cases with dextrocardia and situs inversus there is not true mirror-image dextrocardia. Brown (1950) says that in isolated dextrocardia the aortic arch is more often left- than right-sided when the cavities are inverted and usually left-sided when they are not.

We do not think there is any constant relationship, but a left-sided aortic arch is more common with isolated dextrocardia and a right-sided arch with isolated lævocardia (Table III).

Discussion

The four basic anatomical patterns that are most usual are shown in Fig. 2, which indicates diagrammatically the position of the ventricle, the venous atrium, the superior vena cava, the aortic arch, and the stomach as representing the abdominal viscera. Most commonly the aortic arch and the superior vena cava follow the abdominal viscera, though there are exceptions where one or other or both follow the heart rather than the other viscera.

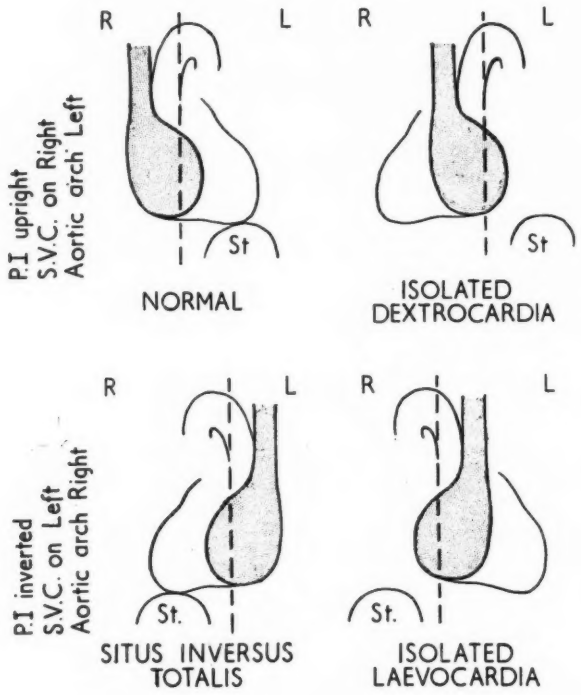

Fig. 2.—Diagram of the four most common relationships of the heart and vessels to demonstrate the position of the superior vena cava, of the venous atrium, of the ventricles, and of the aortic arch. St. = stomach. The pattern shown for isolated lævocardia is the least constant of these.

The venous atrium always appears to follow the superior vena cava and for this reason the direction of the P wave in lead I will show whether they are in their normal position or transposed. The ventricles are not always transposed when the atria are: being the main part of the heart they must generally lie as the heart appears to.

This is supported by the electrocardiographic pattern of QRS. The QRS complex of lead I of a mirror-image dextrocardia normally shows a Q wave, which may not, however, be predominant when the venous ventricle is hypotrophied. Among our 11 cases of dextrocardia with complete situs inversus this was so in every case. A QI was also present in 10 of the 15 cases of isolated dextrocardia, including 7 of the 12 where PI was upright; this suggests, as does their anatomical position, that in these at least the ventricles were transposed while the atria were not. On the

other hand a QI was present in only 4 of the 14 cases of isolated lævocardia, including only 2 of the 6 where PI was inverted, which suggests that in the others normally placed ventricles were associated with transposed atria. In those cases where the form of the QRS complex does not tally with the anatomical position of the ventricle, it may be that the ventricles are rotated rather than transposed.

The main exceptions to the patterns shown in Fig. 2 are found in the group with isolated lævocardia. Here only about half the P waves point in the direction that might be expected. Presumably in the other half the venous atrium (and perhaps the superior vena cava) has not been transposed but has remained in its normal position as the rest of the heart has.

Forgacs (1947), developing the suggestion of Lochte (1898), thought that there was transposition of the atria in most of these cases. Possibly, when there is an upright PI in isolated lævocardia the venous atrium has not been transposed, i.e. has followed the ventricles and not the abdominal viscera. On the other hand, the cases with an inverted PI are those that have followed the pattern shown in our Fig. 4 and here the atrium is anatomically transposed, as suggested by Forgacs (1947). It will be interesting to see when more cases have been fully investigated by angiocardiography or post mortem, if anatomical support for this view can be obtained.

Since writing this we have seen a recent book by Soulié (1952). In the cases of situs inversus with dextrocardia he, of course, expresses the orthodox view, but adds:

" Ce signe (une onde PI négative) n'est pas absolument pathognomonique: il a été observé dans quelques cas de cardiopathies congenitales sans situs inversus."

In isolated dextrocardia without transposition of the viscera, he states: " l'onde PI demeure toujours positive," and with this we are in agreement in so far as it includes all those cases where the superior vena cava also is not transposed. Finally, in lævocardia without transposition of the abdominal viscera he says: " L'electrocardiogramme peut montrer, comme dans le situs inversus avec dextrocardie, une onde PI négative."

Doliopoulos and Maillet (1952) have reported 5 cases of their own of isolated lævocardia and discuss 34 reported cases. Although according to them negativity of PI was considered to be pathognomonic of inversion of the auricles, they concluded that this view was not really supported by the cases reported, without presenting any convincing evidence for this conclusion. Electrocardiograms were available in only a proportion of the cases they considered. In 16 where the diagnosis was not proved by necropsy the P wave in lead I was inverted in 4, and in 4 cases where the diagnosis was supported by necropsy PI was inverted in one and isoelectric in one.

Conclusions

Cyanotic congenital heart disease is not uncommon in dextrocardia with situs inversus. Here the P wave in lead I is generally inverted, as in normal situs inversus totalis.

Cyanotic heart disease is almost universal in isolated dextrocardia without transposition of the abdominal viscera and in isolated lævocardia with transposition of the viscera.

In isolated dextrocardia the P wave in lead I is most often upright. It is always upright in those cases where the venous atrium and the superior vena cava have remained in their normal position.

In isolated lævocardia the P wave in lead I is often inverted. It is always inverted in those cases where the venous atrium and the superior vena cava have been transposed with the abdominal viscera. However, this pattern is found less constantly in isolated lævocardia than the opposite pattern in isolated dextrocardia.

An upright PI with inversion of PII and PIII is another common pattern in isolated lævocardia. This may be because the sinu-atrial node lies low in the atrium, adjacent to the coronary sinus.

The side of the aortic arch will give some clue to the probable anatomical arrangements but less constantly than the side of the superior vena cava does.

References

Beaujeu, A. J. de, and Bège, R. (1937). *Arch. Mal. Cœur*, **30**, 977.
Brown, J. W. (1950). *Congenital Heart Disease*. 2nd ed., Staple Press, London.
Campbell, M., Gardner, F., and Reynolds, G. (1952). *Brit. Heart J.*, **14**, 317.
Campbell, M., Reynolds, G., and Trounce, J. R. (1953). *Guy's Hosp. Rep.* (in the press).
Doliopoulos, T., and Maillet, J. (1952). *Cardiologia*, **20**, 80.
Donzelot, E., Emam-Zade, A., de Balsac, R. H., and Metianu, C. (1949–50). *Acta med. scand.*, **136**, 13.
Forgacs, P. (1947). *Brit. Heart J.*, **9**, 27.
Grieshaber, H. (1936). *Schweiz. med. Wschr.*, **66**, 1307.
Lichtman, S. S. (1931). *Arch. intern. Med.*, **48**, 683.
Lochte, —. (1898). *Beitrag. path. Anat. allg. Path.*, **24**, 187.
Röesler, H. (1930). *Wien. Arch. inn. Med.*, **19**, 505.
Ruskin, A., Tarnower, H., Lattin, B., and Robb, G. P. (1943). *Amer. Heart J.*, **25**, 116.
Shaw, E., and Blake, H. K. (1924). *Amer. J. Dis. Child.*, **28**, 204.
Soulié, P. (1952). *Cardiopathies Congénitales*. L'Expansion Scientifique Française, Paris.
Taussig, H. (1947). *Congenital Malformation of the Heart*. Commonwealth Fund, New York.
Thomson, J. (1950). *Brit. Heart J.*, **12**, 147.
White, P. D. (1951). *Heart Disease*. 4th ed., The Macmillan Co., New York.
Wood, P. (1950). *Diseases of the Heart and Circulation*. Eyre and Spottiswoode, London.
Young, M. D., and Griswold, H. E. (1951). *Circulation*, **3**, 202.

THE SURGICAL AND PATHOLOGICAL ANATOMY OF THE MITRAL VALVE

BY

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The great practical importance that mitral valve disease has now assumed in surgery demands a consideration of the anatomy and function of the normal valve and the pathological anatomy of the diseased valve. Observation on many normal and diseased specimens and direct study of the valve at some 150 operations has made it clear to me that much that is now taught is quite unacceptable. The revision and extension of existing knowledge has often been seen in the development of the surgery of all parts of the body; relatively recently we have seen the great expansion of pulmonary surgery and the corresponding intensive study of pulmonary anatomy and pathology.

In considering valvotomy for the relief of mitral stenosis we are too inclined to concentrate our attention on the valve cusps, forgetting that they are but one part of the valve mechanism. Although the complex nature of the valve mechanism is well known it seems to be largely ignored in dealing with the diseased valve, which is often approached as merely a fibrous, obstructing diaphragm with a small hole that must be made larger. The popular conception of the valve in mitral insufficiency seems to have no logical or scientific basis and is wholly unsatisfactory.

The valve mechanism extends over a distance of some 5 cm., and a lesion may affect all parts of it or one part more severely than another. A lesion at any level can seriously interfere with the mechanism, and it is not always the actual valve cusps that are most seriously affected.

The Normal Mitral Valve

The normal mitral valve consists of the atrio-ventricular fibrous ring to which the cusps gain their attachment, of the two cusps, and of the papillary muscles with their chordæ tendineæ. The two cusps are anteromedial and posterolateral, being so arranged that the axis of the valve orifice is directed obliquely forwards from right to left (Fig. 1, 18, and 22).

The *anteromedial* or aortic cusp is much the larger and the more important in that during ventricular systole it receives a great part of the stream of emergent blood which it prevents being driven back into the left atrium and helps to direct into the aortic outlet.

The *posterolateral* cusp fulfills a secondary and supporting part in the closing of the mitral orifice in ventricular systole.

The *papillary muscles* are typically two in number and lie opposite the intervals between the valve cusps; they arise from the ventricular wall at about the junction of the apical and middle thirds, one being anterolateral and one posteromedial. Both muscles are situated in the lower inflow portion of the left ventricle; the anterolateral one arising from the concavity of the anterolateral wall of the

FIG. 1. — Diagram of the arrangement of the mitral cusps.

ventricle and the posteromedial from the junction of the septal and posterior surfaces. Each muscle may be a single papilla or may be split to a greater or lesser degree so that it is either notched at its apex, deeply grooved along its sides, or bifid. Extra muscles may exist. Rusted *et al.* (1951) have recently analysed the arrangement of the paillary muscles in 250 hearts.

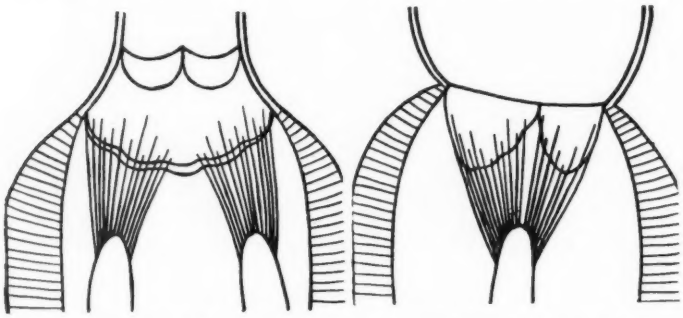


FIG. 2.—Diagram of the arrangement of the papillary muscles and chordæ tendineæ. Each muscle and its tendons controls the corresponding half of the opposing cusps.

The *chordæ tendineæ* pass from each papillary muscle to gain attachment to both valve cusps in such a way that the anterolateral muscle and its tendons control the anterolateral half of the valve, and the posterolateral muscle and its tendons control the corresponding posterolateral half (Fig. 2, 3, and 5). The chordæ tendineæ are of three orders, according to Quain (1929).

(1) Those which are inserted on the free edge of the cusps. They are numerous delicate threads which arise from the other cords near the cusp margin, and often form a fine network before they are attached to it.

(2) Those which are inserted at intervals on the ventricular surface of the cusp near its free edge, which they pass over to the attached border. They are distinctly thicker than the chordæ of group 1, and those attached to any one cusp are derived from two different papillary muscles or from one papillary muscle and the wall of the ventricle.

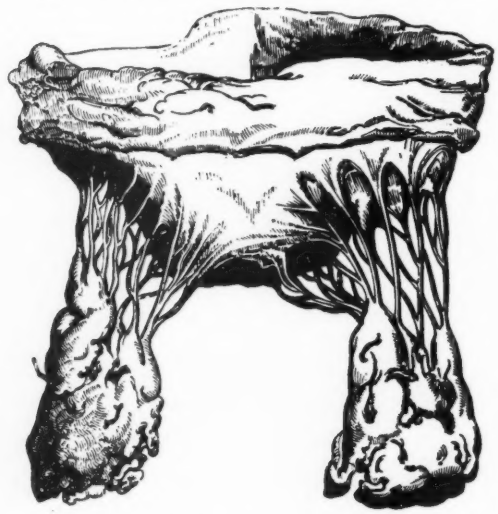


FIG. 3.—The mitral valve. Reproduced from an article in the *Guy's Hospital Reports*, by T. Wilkinson King, 1840.

(3) The short, broad fibres that stretch across the perivalvular groove from the ventricular wall to the under surface of the cusp near its base and run along the cusp a short distance towards its free margin.

The Critical Areas of Tendon Insertion

Although the arrangement of the chordæ tendineæ can be correctly described in this fashion, the total picture presented is too complex—too complete—for practical purposes. It needs simplification. Study of the arrangement has impressed me with the essential importance of the direct or primary attachment of the tendons.

The primary attachments are two on each

cusp, being situated about 2 cm. apart; these I have termed *the critical areas of tendon insertion*, for reasons which will become apparent later.

These areas are depicted in Fig. 4 and 5 and are seen to be formed by those tendons that arise from the very summit of the papillary muscles and gain the most direct attachment to the valve cusps. These tendons are often slightly thicker and stronger, and clearly must exercise the most powerful selective action on the cusps since they are in the line of the direct pull of the papillary muscles. The more obliquely placed tendons which gain insertion on each side are of a secondary supporting nature.

The disposition or shape of the cusps is such that there exists, fundamentally, a distal or central horizontal portion and two lateral or receding oblique portions. The critical areas of tendon in-

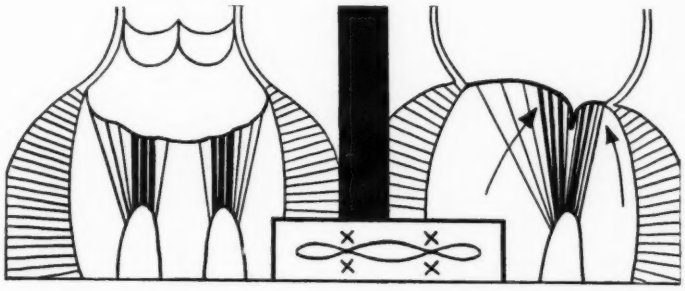


FIG. 4.—Diagram to show the probable mode of closure of the mitral cusps. The thicker chordæ tendineæ are those in the direct line of pull from the papillary muscle to the cusps. The small inset indicates the critical areas of tendon insertion thus formed; in these areas the cusps are held most tightly together.

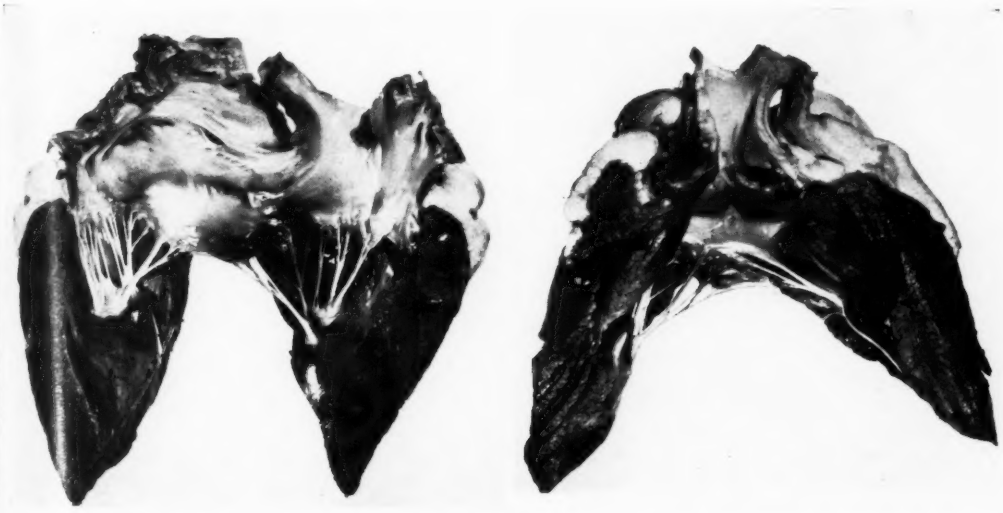


FIG. 5.—Photograph of bullock's heart opened to show the mitral cusps. The arrangement of the tendons from each papillary muscle controlling half of each cusp is well shown. The large, prominent cusp is the anteromedial or aortic, and the critical areas of tendon insertion should be noted with the central blood pathway between.

sertion are at the junction of the horizontal part and the lateral receding parts of the valve cusps. Most of the oblique or secondary tendons are inserted in relation to the lateral parts of the cusps; fewer pass medially to what may be termed the central pathway of the valve (Fig. 3 and 5). This is especially so in the case of the anteromedial cusp. It is true that the shape of the free edge of the cusps may be described as semicircular or semi-ovoid, but the above suggested resolution into a somewhat arbitrary transverse or horizontal distal central portion and the two lateral receding portions is of great practical importance and, I think, aids clarity of understanding.

The Closure of the Normal Mitral Valve

Although the mode of closure of the mitral valve may appear to be fairly obvious and simple, it is a good policy to take nothing for granted but to re-examine the existing conceptions from time to time. Actually, there is room for considerable difference of opinion in the exact mode of closure of the valve.

It is almost certain that the two cusps come together along their opposing surfaces, being driven into this position by the rise in pressure during ventricular systole (Fig. 4). The anterior cusp is 15–18 mm. long at its middle part and the posterior cusp is 10–12 mm. The extent of their probable contact can be judged from the observation (Quain, 1929) that the area of the atrioventricular orifice is 855 sq. mm. in a man and the surface area of the two cusps is 1868 sq. mm. The proportion of valve area to orifice area, therefore, appears to be from 1:1·5 to 1:2·2. The overlap may, in fact, be more than this, because when the ventricle contracts the A-V ring is reduced in circumference and the area of the orifice is correspondingly reduced.

On the other hand Quain does not state the conditions under which these measurements were obtained, although presumably in the cadaver, and we must make allowance for much variation in the degree of contraction and dilatation of the heart and mitral orifice that may be present, whether caused by disease or by *rigor mortis* affecting the heart muscle. Nature is always prodigal in her reserve and it may well be that the overlap described above pertains to quiet resting conditions of the healthy heart, but is greatly lessened during exercise or illness, especially when the heart muscle is affected by the disease.

A possible alternative mechanism of closure is that the orifice is closed entirely by the anteromedial or aortic cusp forcing the much smaller posterolateral cusp against the posterior wall of the ventricle (Fig. 6). It is doubtful if this is the usual mechanism, but it may well happen sometimes; it is unlikely to occur if the A-V ring is at all dilated. In systole the inflow portion of the left ventricle is tightly contracted so that its cavity is almost completely obliterated, but sufficient space remains postero-inferiorly for the hydrostatic pressure to reach the ventricular aspect of the posterolateral cusp and force it away from the wall of the ventricle. The greater part is in contact with the opposing surface of the aortic cusp and its " free " area must be small. When the finger is introduced into the left atrium during an operation for mitral stenosis, the anteromedial cusp is usually very easily felt billowing upwards into the atrium like a sail filled with the wind; it is much more difficult to feel the posterolateral cusp, and, indeed, its presence has often rather to be assumed by judging the distance that lies between the actual mitral orifice and the posterior part of the A-V ring.

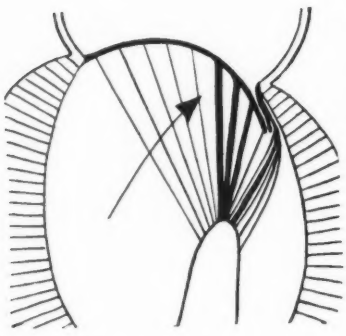


FIG. 6.—Diagram to show a possible alternative mode of closure of the mitral valve in which the posterolateral cusp is forced against the wall of the ventricle by the anteromedial cusp.

Lutembacher (1950) describes the mechanism of closure as a bunching up in which the valve cusps, the chordæ tendineæ, and the papillary muscles come together in such a way that the closure of the orifice is aided and secured by an actual interlocking or interopposing of these structures, and he describes and depicts specimens in such a way as to indicate that the partly cockled-up mitral orifice in mitral stenosis actually occupies grooves on the papillary muscles.

This is a conception reached by inspection of the dead contracted heart; from what the finger feels when inside the contracting heart it cannot be a true one. I have felt the mitral valve functioning on some 150 occasions and the aortic cusp at least has always been forced or billowed towards the atrium; it has never been gripped or bunched up within the orifice.

Although it is difficult to feel the posterolateral cusp billowing out, it would be strange if it did not do so in conformity with the aortic cusp, for the very presence of the musculo-tendinous mechanism indicates that this is the action of the cusp in systole. It cannot fail to be forced upwards and backwards in this manner unless it is entirely protected from the high ventricular systolic pressure by complete apposition with the posterior wall of the ventricle.

There is little doubt that the aortic cusp is the main factor in effective closure of the orifice and the posteromedial cusp occupies a subsidiary or adjuvant function in sealing a narrow and probably variable posterior crescent of the orifice. The variability of its apposition with its fellow cusp in varying degrees of cardiac activity or dilatation has already been mentioned.

According to Quain the distance between the apex and the base of the left ventricle does *not* shorten during contraction of the ventricle; the atrioventricular region moves upwards and backwards, but the length of the cavity remains constant. This makes it easier to understand how the comparatively small contraction of the papillary muscles is able to ensure efficient closure of the valve. Actually, all that is needed is quite a small tensing of the chordæ tendineæ to prevent the cusps being blown open into the atrium. The apposition of the cusp surfaces ensures their watertight closing, but the pressure-resisting mechanism comes from the musculo-tendinous support and its neuromuscular co-ordination with ventricular systole. The mode of insertion of the tendons from one papillary muscle to each of the opposing cusps increases the efficiency of the mechanical closure of the valve.

The important, indeed fundamental, part played by the papillary muscle mechanism was dramatically, albeit tragically, emphasized for me in one unfortunate operative experience (Brock, 1950). After dividing the stenosed orifice in a case of mitral stenosis I tried to reach the aortic valve by passing the index finger around the aortic cusp of the mitral valve. I had just reached the valve with the finger-tip when something gave way and immediately severe mitral regurgitation occurred; a powerful regurgitant stream of blood could be felt entering the atrium, the walls of which could be seen to distend freely with each ventricular systole. Clearly the high ventricular pressure was being transmitted directly to the left atrium. I thought that the aortic cusp had been torn transversely across its substance. The patient, unable to tolerate this severe acute mitral incompetence, died some 48 hours later and autopsy revealed that the anterolateral papillary muscle had been torn from its ventricular attachment; the simple mechanical apposition of the two cusps had not been enough to prevent the severe and fatal regurgitation.

During ventricular diastole the papillary muscles and the tendons are lax and the cusps float open before the stream of blood from the atrium. During ventricular systole the valve cusps are flung tight together and the papillary muscles and tendons become taut and straight; the maximum, the most powerfully supported, closure must occur in relation to the critical areas of tendon insertion already described. At the height of systole the tendons passing from the summit of each papillary muscle direct to these two critical areas on the valve cusps must be tense and parallel and very close to one another (Fig. 4); in contrast with during diastole when they are lax and directed outwards towards the wide open margins of the orifice. At these two critical areas the cusps must be held together very tightly indeed; the significance of this will become apparent when we consider the state of the diseased valve. Sokoloff *et al.* (1950), as a result of a study and survey of the chordæ tendineæ in 200 hearts of all ages, have shown that the more centrally placed chordæ of the anterior cusp are thickened and more powerful in every heart and this can be noted at all ages and in animals (bovine) when rheumatic infection can be excluded. The changes are less marked in the chordæ of the posterior cusp, as would be expected.

The size of the mitral orifice. I have always been intrigued by the difference in size between the A-V orifice and that of the aorta or pulmonary artery. The explanation that first suggests itself is that this is related

to the lower pressure in the atrium. This may be so except that nature could just as easily have made the atria slightly more powerful without interfering with any venous reservoir or volume-regulating function they may possess. After all the blood has only to be expelled into the lax ventricular cavity during the long diastolic filling period; the atria do not have to maintain a systemic or even a pulmonary blood pressure such as the ventricles must do.

I do not believe that the real difference in size between the atrial and the aortic orifices is anything like so great as appears. The explanation is that only a part of the A-V channel functions as a true pathway for the blood; this soon becomes apparent when the mechanism of the normal mitral valve is considered more closely.

Quain gives the size of the aortic and the mitral orifices in mm. as follows:

Aortic orifice: 26 mm. in diameter, 530 sq. mm. in area
Mitral orifice: 32 mm. in diameter, 855 sq. mm. in area

We are thus faced with an apparent difference in size which is indicated by the diagram shown in Fig. 7. The mitral orifice has not been depicted as a circle in spite of the figures given above, for in fact it is usually not circular during life.

If, instead of simply superimposing the two " orifices " in this way, we consider them in the form shown in Fig. 8, we obtain a different conception which is best explained by developing the diagram further to present the basic structure of the mitral valve already mentioned. That is, a distal horizontal or central portion and two receding lateral portions; at the junctions of the central and lateral portions are the critical areas of tendon insertion (Fig. 8 B).

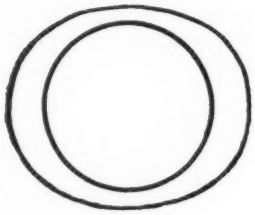


FIG. 7.—Diagram to contrast the relative size of the mitral and the aortic orifices.

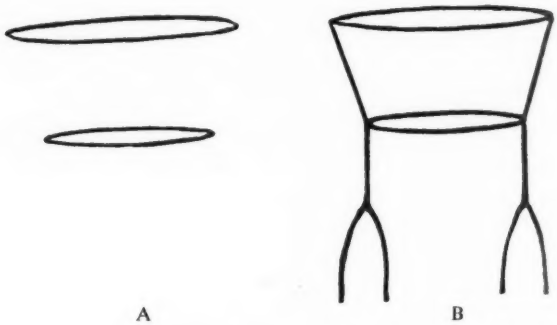


FIG. 8.—Diagram to illustrate the suggested mode of construction of the mitral pathway.

We may now return to a diagrammatic representation of the mitral orifice from above (Fig. 9) with the valve in the open and in the closed state. Although the orifice may be thought to open as a simple oval, it will be seen that this is, in fact, not so. The part of the valve orifice that matters is what I would term the central channel and it is formed by the opening of the distal, horizontal, central portions of the cusps. The receding lateral portions serve merely as hinges, allowing the central portions to open and close. Indeed, the two " lateral " parts of the valve channel on each side of the central channel are largely filled in, when open, by the numerous chordæ tendineæ radiating, fan-wise, upwards and outwards from the papillary muscles (Fig. 3). The tendons passing to the borders of the central channel are fewer and are disposed so as not to interfere with the blood pathway.

It will thus be seen that the effective orifice of the mitral valve is much smaller than would at first appear, and is much more closely related to that of the aortic orifice. The apparent difference in size is due entirely to the essentially different mechanisms in the opening and closing of the aortic valve and the mitral valve. McMillan *et al.* (1952) have recently demonstrated that the functional aortic outlet at the valve level is triangular and not actually circular.

THE DISEASED MITRAL VALVE

It is usually taught that in the milder forms of rheumatic infection the edges of the mitral cusps become thickened and distorted and some incompetence results; and that with a more severe

infection the valve cusps adhere, the orifice becomes contracted, and stenosis follows. Examples are depicted in text-books of valves, said to be incompetent, in this lesser state of thickened, distorted edges. In this way many students gain the impression that mitral incompetence results from a mild rheumatic valvitis, and stenosis from a more severe attack. This is an erroneous simplification; a high degree of mitral stenosis can be caused by a relatively mild attack of rheumatic valvitis; in contrast, true mitral incompetence is usually caused by the most severe grades of damage to the valve. The condition of the thickened, deformed edges with no fusion of the cusps is, almost certainly, of little or no functional significance.

Study of diseased mitral valves teaches that considerable varieties and degrees of valvitis occur. Although a clinical state of " mitral stenosis " may be present, the actual condition of the valve mechanism varies greatly from case to case and with corresponding differences in the degree of benefit that can follow operation. The valve orifice may be equally small in two cases, but in one the valve cusps may be thin and almost normal and a successful valvotomy will restore an almost normal valve; in the other the whole valve structure may be so altered, so rigid and fibrous, that no more than a partial restoration of function is possible.

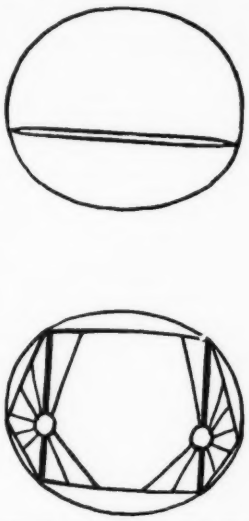


FIG. 9.—Diagram to show the mode of action of the mitral cusps. The true functional pathway is the central portion; the lateral portions serve as hinges allowing the central part to open and close. The thickened chordæ tendineæ indicate the critical areas of insertion; lateral to these the pathway is closed by the lattice work of the supporting oblique tendons. Note the effective central pathway is much closer in size to that of the aortic pathway; cf. Fig. 7.

It is necessary to draw attention to the loose use of the terms mild or severe mitral stenosis. The picture often conveyed, and intended, by such expressions is that the actual degree of contracture of the orifice may be slight, moderate, or severe. This is not in accordance with operative experience; the mitral orifice in stenosis is almost always a small oval about 1 cm. × 0·5 cm.; in a small percentage of cases it may be very much smaller and is then usually circular, as little as 0·4 cm. in diameter.

It is, however, not possible to explore case after case and observe the almost standard small orifice, 1 cm. × 0·5 cm., without being impressed by its occurrence and significance. The same small orifice is found in cases with mild symptoms or with severe symptoms. It is not the mitral stenosis that is mild or severe; it is the resulting disability. The anatomical variation in the size of the hole is slight; the clinical variation of symptoms is considerable. It would seem that a certain minimal size of valve orifice must be reached before clinical disability is likely.

This has an important practical bearing for two reasons. First, just because a patient has early symptoms of mitral stenosis it is not to be assumed the orifice is only mildly contracted; at operation it will be found little or no different from that found in a severe case. The patient with mild symptoms can expect to receive just as much mechanical relief by valvotomy as one with severe symptoms. Second, the anatomical occurrence of this virtually " standard " type of orifice in mitral stenosis demands an explanation based on sound pathological anatomy.

THE MECHANISM OF PRODUCTION OF MITRAL STENOSIS

Rheumatic inflammation occurs firstly and chiefly along the margins of the valve cusps; if the cusps remain separate and only the margins are affected, the final result is merely some permanent thickening and mild distortion of the edges of the cusps, a condition of no functional importance.

The significant event in the production of mitral stenosis is the fusion of the valve cusps *and this occurs, fundamentally, at the two opposing critical areas of tendon insertion* (Fig. 10A). It must be

emphasized that in an appreciation of this simple fact lies the correct understanding of the production, the anatomy, and the technical operative treatment, of mitral stenosis.

It is in these areas that the inflamed cusps are held most tightly together in systole; once cross adhesion has occurred, important secondary changes follow, for the hinge-like action of the lateral parts of the valve cusps is at once lost. In other words, the opening of the central pathway in diastole is prevented; the valve cusps cannot move apart, held as they are by the cross fusion at these critical sites. The central pathway—functional lumen of the valve—must inevitably remain partly open if life is to continue, but its size is inevitably no more than a shallow oval formed between the two areas of adherence at the critical points (Fig. 10B).

To the outer side of each critical area, i.e. on each side of the central pathway, the valve lumen is now functionless, it does not form part of the main blood channel from atrium to ventricle, and

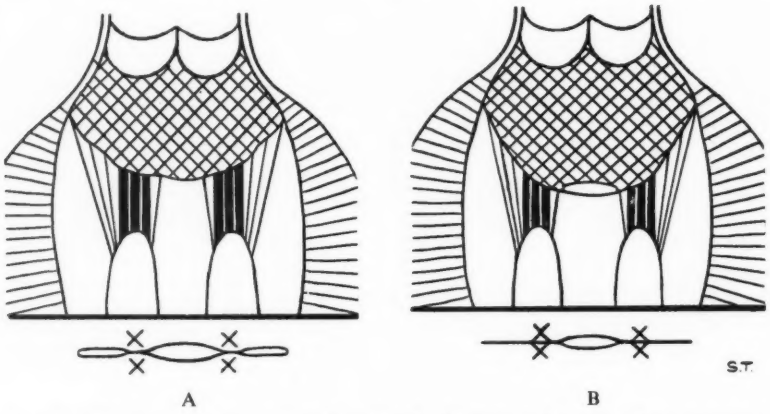


FIG. 10—Diagram to show suggested mode of adherence and fusion of the cusps and consequent production of mitral stenosis. In A the inflamed cusps adhere first of all at the critical areas. In B complete cross fusion of the critical areas has occurred, and also secondary adherence of the commissures.

as already pointed out, it really exists only to allow complete opening of the central part of the valve lumen or pathway in diastole. Once the two lateral components are prevented from opening in this way by the cross fusion of the critical areas of tendon insertion it is inevitable that they should completely fuse together since there is no powerful direct stream of blood to keep them apart. In this way the two " commissures " are formed; i.e. the cusp margins are fused from the atrial ring up to and including the two critical areas of tendon insertion (Fig. 10B).

The commonly accepted notion that stenosis arises from progressive fusion of the cusps, beginning at the periphery and extending inwards, is quite erroneous. Cases of mitral stenosis with partial lateral adherence of the cusps with non-adherence of the " critical " areas just do not occur. It is true that the orifice may be eccentrically placed and one commissure may be much shorter than the other or both may be very short, but this is due to variation in the focal incidence of the infection which may produce a more severe degree of inflammation in one place and therefore greater local contracture.

Once cross adhesion of the critical areas and secondary adhesion of the commissures has occurred, a state of mitral stenosis inevitably results. The degree of stenosis must clearly depend on the size of the oval aperture that is subtended between the fused critical areas. In the earlier stages, or in cases in which the valvitis is mild, this central lumen may be rather larger than in other circumstances, but is never likely to be more than about 1·5 cm. × 0·75 cm.

If the valvitis is severe, recurrent, or chronically smouldering, this central lumen is likely to become rapidly much smaller and with correspondingly more rigid margins. Symptoms may then occur early.

If the valvitis ceases quickly and the patient is left with a small functional oval lumen some 1 cm.–1·5 cm. in length and with fairly supple margins, although stenosis is present, symptoms may be completely absent. With a healthy muscle there is little doubt that considerable stenosis of the central pathway of the mitral valve can be readily compensated for. Symptoms could appear if the muscle begins to weaken, but the more likely cause is a steady diminution in the size of the valve lumen until it reaches what might be termed the minimal effective area. This seems to be the small oval aperture most commonly seen, some 1 cm. × 0·5 cm.; if the lumen becomes smaller than this graver symptoms can only be forestalled by a correspondingly greater increase in the power of the atrial muscle and the increased risk of its failure.

The steady diminution in size of the central lumen towards the minimal effective area, if not caused by actual rheumatic infection, is inevitable from the daily wear and tear of the blood stream passing through the narrowed orifice, especially as the wear and tear or friction is steadily increased by the stronger flow of blood brought about by the more powerful contractions of the partly obstructed left atrium. By the deposition of platelets and fibrin the edges become thicker, more fibrous and therefore more contracted and rigid and the orifice correspondingly smaller; verrucose projections and even calcified plaques and masses add further to the obstruction. This progressive and relentless shrinkage of the functional central lumen over the course of the years is one main reason why the appearance of symptoms in mitral stenosis is closely related to increasing age and is commonest between 30 and 40 years. Clearly the condition of the atrial muscle is also important in this connexion.

Just as the edges of the valve opening are exposed to the wear and tear of the blood stream, so are the chordæ tendineæ in the direct line of pull from the papillary muscles, as these inevitably form part of the banks confining and directing the stream of blood issuing from the stenosed orifice. It would therefore be expected that these chordæ should show extra evidence of thickening all along their length. This is indeed so and Sokoloff *et al.* (1950) have drawn attention to the occurrence of sclerotic changes in these central chordæ tendineæ, especially of the anterior cusp, in the heart of middle-aged subjects who were not rheumatic; the sclerosis is due to deposition of subendocardial collagen and affects the whole length of the chordæ and more particularly the central ones which are more exposed to the mechanical action of the blood stream. Magarey (1951) has also written of this.

Mitral Stenosis with Minimal Valvitis

The basic mechanism of valve fusion, beginning with cross adherence of the critical areas and extending by more gradual secondary narrowing of the central pathway, is seen most clearly in cases in which the rheumatic infection has been confined almost entirely to the valve margins. The patient's symptoms may be severe ; the central orifice characteristically small, 1 cm. × 0·5 cm. or even less, its edges firm and fibrous; in other words the stenosis is severe. The condition of the valve cusps themselves, however, shows that the original rheumatic infection was not severe; or at least did not affect the whole valve cusps but chiefly the margins. Although the edges of the central orifice may be firm or even dense, the fusion of the critical areas is not densely fibrous, the commissures are often very lightly fused, and the actual valve cusps are thin, supple, and almost normal. Moreover, the chordæ tendineæ are thin and separate and once the two cusps have been separated (by splitting or cutting) as far as the A-V ring on each side, an almost normal valve mechanism is restored.

It is noteworthy that a patient can have such a severe disability, eventually fatal, from a simple cross fusion of the cusps following what must have been a mild form of valvitis and that this great disability can be quickly relieved by a short and simple operation.

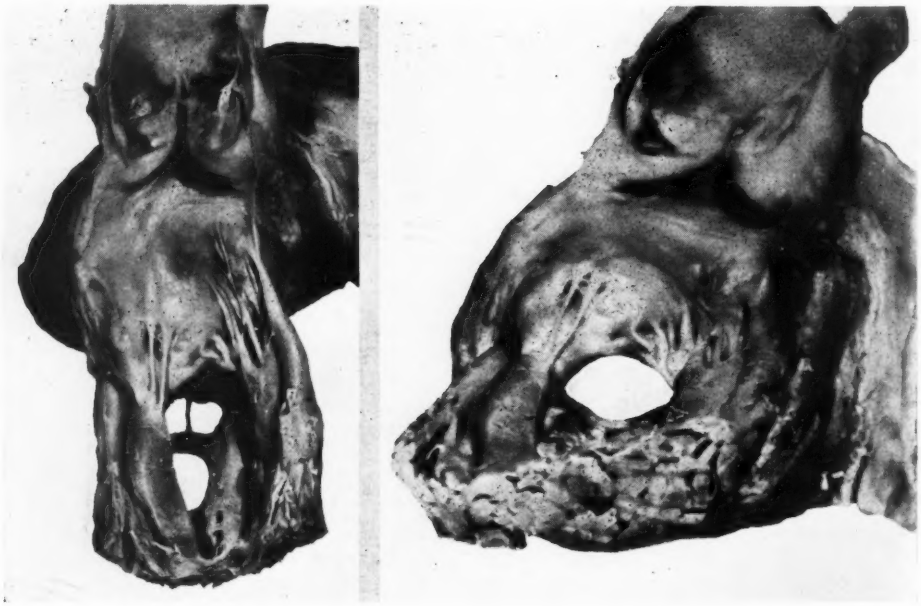
Mitral Stenosis with Severe Valvitis

In the more severe grades of rheumatic valvitis the process is no longer confined to the margins but spreads to involve the cusps, the chordæ tendineæ, the A-V ring and even the papillary muscles. The cusps become generally thickened and fibrous so that they constitute a rigid or semi-rigid fibrous diaphragm with a small rigid orifice. Calcification may also be added, either in the form of light surface deposit or thick plaques or exuberant craggy masses.

The chordæ tendineæ become thickened, matted together, and shortened; in extreme cases the fibrous reaction extends down to involve the papillary muscles, and the chordæ may then be so shortened that the papillary muscles are almost directly fused with the valve cusps themselves, only a short thick fibrous mass intervening (Fig. 11, 12, and 13). The papillary muscle and tendons may even adhere to the wall of the ventricle. Occasionally calcification extends from the valve cusps and the orifice, down the chordæ tendineæ as far as the papillary muscles, so that a narrow calcified channel is formed. The fibrosis may also involve the A-V ring, which becomes smaller and rigid, and in some cases actually calcified.

These facts are, of course, common knowledge, but it is necessary to consider more critically the precise effect on the chordæ tendineæ. The most important change occurs in those tendons directly inserted into the critical areas.

The primary fusion of the cusps in these areas has been described; in mild forms of inflammation the chordæ are not fused, or only lightly, so that if the adherent cusps are divided the valve orifice can immediately open widely or will do so if the lightly fused tendons are separated with the finger. When, however, the valvitis is severe, the primary groups of tendons inserted into the critical areas become fused firmly to one another and *cross fusion also occurs between the sets on each side of the valve cusps*. Thus, to the fusion of the cusps or commissures is added a dense fusion of the



A B

FIG. 11.—Photograph of stenosed mitral valve to show the matting and shortening of the chordæ and, in the view from below, (B), the narrowed residual central pathway between the two flanking, fused critical areas of tendon insertion.

FIG. 12.—Photograph of a severe form of mitral stenosis in which the cusps are very densely fibrous and the fused chordæ tendineæ at the critical areas form a thick solid mass of fibrous tissue more than 1 cm. in thickness in each direction. At operation it was not possible to enlarge the stenosed orifice further than this strong barrier on each side. Even if the barrier had been cut through, the fusion down to the papillary muscles would have prevented the cusps from opening. Carrying the incision round the fused tendons would have destroyed the support of the cusps and caused severe regurgitation. It is in this type of valve that secondary narrowing of the orifice, i.e. recurrence, is inevitable, although it may take some time to become of clinical importance.

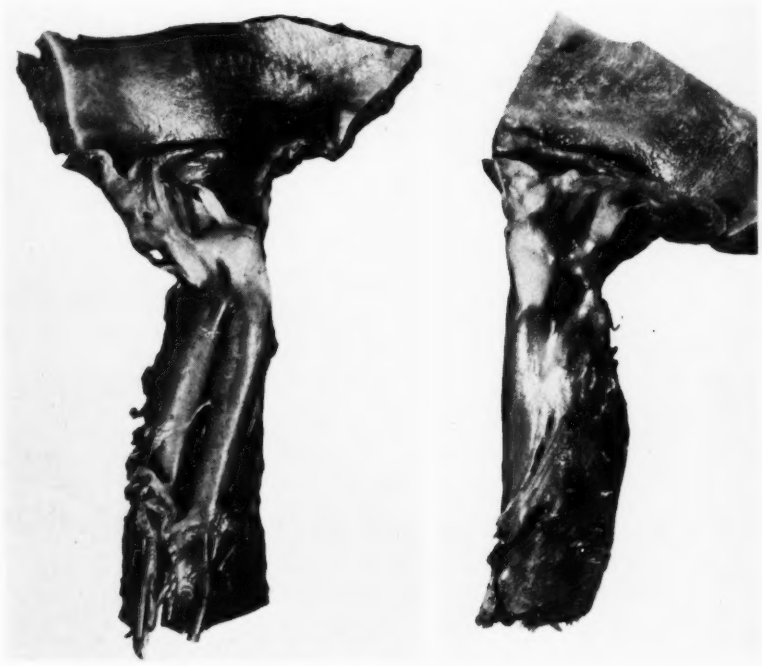


FIG. 13.—Photograph of a grossly scarred and virtually disorganized valve. Such severe changes and dense fusion make a condition that is virtually inoperable.

tendons. Even if the fused cusps are cut apart the valve orifice still cannot open because it is held firmly by the fused and interfused chordæ. These may form a solid, thick barrier or column as much as a centimetre or more in both width and thickness (Fig. 12 and 13). This fusion of the primary tendons inserted directly into the critical areas is further reinforced by inclusion of the more obliquely placed tendons so that these now pass straight up to the critical areas and then incline outwards along the under surface of the cusps almost like the fan tracery of Gothic architecture radiating from the supporting columns of the roof (Fig. 14). It is clear that when such a thick, fibrous, fused mass is formed it constitutes a grave obstacle to the effective surgical relief of mitral stenosis. Moreover, the valve mechanism is very badly damaged, although not entirely ruined if incompetence is absent or slight.

Fortunately the more severe grades of valvitis may not always affect the whole of the valve mechanism. Indeed, it is quite common to find that the brunt of the inflammation has fallen chiefly on one part. This may be either the medial or the lateral commissure and the adjacent part, more commonly the medial than the lateral. One commissure may be short and occupied by an exuberant, craggy, calcified mass with dense fusion of the chordæ, while the other is still only mildly affected. It is noteworthy that one effect of valvitis may be to *lengthen* the cusps, especially the anterior or aortic cusp, as a result of extension of exudate and its organization along the chordæ

FIG. 14.—A Gothic column with fan tracery to recall the solid fusion of chordæ tendineæ and their radiation beneath the cusp. Reproduced by the courtesy of Messrs. Thames and Hudson, from *English Cathedrals*, by Martin Hürlimanm.

FIG. 15.—Photograph of specimen of mitral stenosis to show the way the aortic cusp becomes lengthened as a result of organization of exudate extending into the chordæ.

tendineæ from the free margin of the valves (Fig. 15). This process also contributes to the secondary shortening of the tendons (Fig. 11, 12, and 15). It is in contrast to the *shortening* of the cusps observed in cases of mitral regurgitation.

Mitral Regurgitation

The diagnosis of mitral regurgitation, formerly made with such confidence, is now accepted as a matter of greater difficulty. The operative treatment is even more difficult. It is obviously essential, in order to make our task easier in these two matters of diagnosis and treatment, to begin with a clear conception of the pathological anatomy of the incompetent valve.

I have already referred to the common error in teaching that a mild rheumatic valvitis, by distorting the edges of the cusps, can cause incompetence at a stage earlier than the production of mitral stenosis. This encourages the idea that mitral incompetence is a milder lesion than mitral stenosis. There is no doubt that this is wrong, both clinically and pathologically. Clinically mitral regurgitation can cause some of the severest forms of cardiac disability. Pathologically it is the result of the severest forms of damage to the valve mechanism, often being associated with complete or almost complete ruining of the valve as a valve. In mitral stenosis, in contrast, even though the degree of obstruction may be severe, the damage to the valve mechanism may be slight and, once the fused valve cusps have been separated, an almost normal valve may be restored. This is never the case with mitral regurgitation.

It is helpful, first of all, to consider what changes may cause the valve to be incompetent, and the six following changes will be considered. Frequently more than one, or even several, of these mechanisms may co-exist, although in varying grades of importance.

(1) A hole or defect in a valve cusp.

(2) Rigidity of the margins of the valve orifice preventing its closure.

(3) Rupture of the musculo-tendinous mechanism so that a cusp is unsupported in ventricular systole.

(4) Shortening of one or both cusps so that they cannot meet and overlap.

(5) Shortening of the musculo-tendinous mechanism so that the valve cusps cannot rise and meet.

(6) Extreme dilatation of the atrioventricular ring leading to secondary relative shortening of the cusps.

(1) *A hole or defect in a cusp*

This is not a feature in rheumatic valvitis, but may be caused by ulceration and destruction of the valve in malignant endocarditis. It can also follow ill-conducted surgery when the substance of one of the cusps (especially the anterior) is damaged. A unique, but at the same time informative case is one reported of a young man who sustained a bullet wound of the anterior cusp and died several years later of heart failure from the resultant incompetence.

(2) *Rigidity of the margins*

The orifice in mitral stenosis is typically a small oval some 1 cm. $\times$ 0·5 cm. In most cases the cusps are sufficiently supple to permit closure, either by overlap or by compression of the opening. If, however, the margins are very fibrous or supported by calcium so as to be quite rigid, then the opening will not close completely in systole and some regurgitation occurs. This may also be favoured if the axis of the orifice is distorted so as to present in an unusual direction, e.g. it may be rotated forwards or backwards so as to favour regurgitation. Even if reflux takes place through the full size of the opening it could not be really significant, and in fact the orifice is often made smaller, even though not completely closed, in systole. In other words the reflux is small and although it may add a systolic murmur to the first heart sound, it adds little if anything to the cardiac disability caused by the stenosis. Moreover, when the fused valve cusps are freed by valvotomy the stenosed orifice loses its rigidity and the suppleness of the cusps is usually enough to correct the insufficiency.

Incompetence from this cause is, therefore, scarcely either a clinical or a surgical problem.

(3) *Rupture of the musculo-tendinous mechanism*

This is a rare occurrence from disease, usually cardiac infarction. Death follows within 24 hours. Smith (1950) mentions 33 reported cases and adds two of his own. An example due to rupture of a papillary muscle at operation was mentioned earlier.

(4) *Shortening of the cusps*

The function of the valve cusps is to meet sufficiently to close the mitral orifice during systole; if they are too short to meet and a gap is left between their edges, regurgitation follows. The more severe grades of rheumatic valvitis cause shortening and rigidity of the valve cusps, and hence incompetence. Indeed, it is the cause *par excellence* of the more severe grades of incompetence which cannot occur merely from a minor affection of the contact margins of the cusps. The normal overlap is so great that considerable damage to the whole substance of the cusps is needed.

This factor of cusps, so shortened as not to meet efficiently, is clearly closely correlated with the two remaining factors, especially the next one.

(5) *Shortening of the musculo-tendinous control*

The valve cusps should float widely open in diastole and then in systole are flung up again until the active contraction of the papillary muscles tenses the tendons and holds the flaps secure. If the papillary muscles and tendons are fused into a solid fibrous mass, shortened and densely adherent to the valve, this mechanism is lost. The valve cusps cannot open properly in diastole, neither can they rise properly to close in systole. There is virtually a fibrous ankylosis of the valve mechanism.

The severe grades of rheumatic infection which cause such advanced changes in the chordæ and papillary muscles are just those that cause equally severe rigidity and shortening of the cusps; thus the two factors work together for evil.

(6) *Dilatation of the atrioventricular ring*

The cusps of a normal valve being inextensible it follows, at any rate in theory, that if the A-V ring were to dilate sufficiently the cusps would no longer meet and incompetence would result. It is probable that this does occur in rheumatic or other forms of myocarditis and may be the cause of the systolic murmur.

If the cusps are shortened by disease, regurgitation can obviously occur more readily if the A-V ring dilates. It is, therefore, a secondary or adjuvant factor aiding incompetence and, moreover, can form part of a vicious circle in that the dilatation can cause incompetence; the incompetence further interferes with the efficiency of the heart and further dilatation follows with consequent further aggravation of the incompetence.

It is probable, also, that as the ring and the chamber of the ventricle dilate, factor (5), i.e. relative shortening of the musculo-tendinous control, is added as an aggravating factor.

The Pathological Changes Observed in Mitral Incompetence

It is fairly easy to understand and describe the pathological changes in mitral stenosis because of the opportunity that has occurred to study many cases during life and post mortem. Particularly important is the ability to examine the valve mechanism actually working when the finger is inserted into the left atrium at operation.

In mitral regurgitation, however, the position is somewhat different because far fewer cases of incompetence have been operated upon; indeed, until quite recently, we have carefully avoided operating on any patient in whom a high degree of regurgitation is suspected. Moreover, in the past, there has been poor correlation between proper post-mortem study and clinically observed and significant incompetence. In fact many pathologists and physicians just have not understood the distinction between the purely stenosed, the purely incompetent, or the grossly damaged, incompetent and stenosed valve. This is made obvious in most museums, where it can be seen that almost any diseased mitral valve in which the orifice is reduced in size is usually described as an example of mitral stenosis. This in spite of the fact that the orifice is perhaps 3 cm. long and 1·5 cm. wide. Such an orifice, although smaller than nature designed, does not cause a significant obstruction to the flow of blood from the atrium into the ventricle. Such a valve is a disability from the gross regurgitation that occurs through the relatively large orifice. In contrast, as stated under

factor (1) above, if the stenosis is so severe as to permit very little blood entering the ventricle, it can scarcely allow a significantly greater amount to regurgitate. One element of the valve damage is the complement of the other. If the stenosis is severe, regurgitation must be small; if regurgitation is severe, stenosis must be small. If we reduce it to extremes we have a state of affairs in which the orifice is completely obstructed, i.e. stenosis is total, regurgitation is nil; conversely if the valve is absent, stenosis is nil, regurgitation is total. Midway between these two extremes we find a certain balance in which the stenosis is of moderate degree, probably not of great significance by itself but becoming clinically and functionally important because it is accompanied by a significant degree of regurgitation through the rigid stoma of moderate size.

The number of cases of proven mitral regurgitation that I have been able to examine at operation and at autopsy is relatively small but it has enabled certain conclusions to be drawn—conclusions that may need modification in the light of further experience. I must emphasize that this study has been *based on true incompetence directly observed at operation* when the valve has been examined with the finger. This can surely be the only sound method on which to base a description of mitral incompetence.

Mitral incompetence is observed in the following three forms.

(1) A small regurgitant stream occurring from a small, grossly stenosed, perhaps calcified, orifice (Fig. 16A).

(2) A moderately powerful regurgitant stream occurring from a narrow orifice, but not grossly stenosed; e.g. it may be 1·5–2·5 cm. long and of varying width. Calcification often determines considerable extra reduction in the width (Fig. 16B).

(3) The orifice is large, perhaps 4 cm. × 2 cm., and a powerful current of blood escapes in ventricular systole. To the examining finger the regurgitant stream feels as powerful as if a tap were running. Clearly no stenosis is present as the orifice is at least equal in area to or even greater than that of the aortic outlet (Fig. 16C).

Type 1 can be dismissed at once for reasons already stated. The regurgitation is a relatively minor incident in a high-grade stenosis and it is usually automatically corrected when the cusps are freed by the relief of the stenosis. It is included merely for the sake of completeness and because it has beguiled the thoughts of many away from the really significant problem revealed in the other two forms.

Type 2 is that more commonly seen and represents the most severe grades of damage to the valve by the rheumatic infection. In fact it may be said that the valve as a valve has ceased to exist. The function of a good valve is to let blood pass freely onwards and to prevent its return. If the valve is converted by disease into a rigid diaphragm with a rigid hole so that too little blood can flow through and there is nothing to prevent its flowing back again, the valve may be said to be completely ruined.

The varying proportions that may be assigned to the stenosis and the incompetence from case to case, can be indicated by using the term " mitral valve disease " for some of these examples of

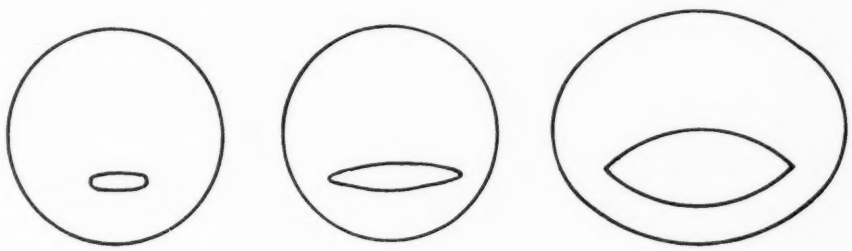


FIG. 16.—Diagram of three types of mitral incompetence; see text.

severe valvular damage exhibited in type 2, rather than using the terms stenosis or regurgitation as descriptive (Bourne, 1952).

The most significant thing the surgeon notices in operating on the cases of mitral valve disease is the importance of the size of the orifice and its correlation with the rigidity or otherwise of the cusps. For instance, in cases of clinically pure mitral stenosis, it is monotonous with what regularity the orifice is found to be some 1 cm. × 0·5 cm. or even smaller: regurgitation is small or absent and depends on rigidity of the edges; the cusps are often thin and supple and the anterior one in particular can be felt to billow freely in systole. In contrasts to scores of this type, one encounters a valve with an orifice that is substantially larger; e.g. 2·5 cm. × 1 cm., with edges that are rigid and fibrous and often grossly calcified. The cusps, too, are rigid and horizontal in both systole and diastole, revealing that movement is slight. A free regurgitant stream is felt during systole and there is often no difficulty in inserting the finger into the orifice and moving it from side to side.

When we examine the valve from such a heart (Fig. 17), we see a state of affairs quite different from that observed in pure mitral stenosis. The most striking feature is total involvement of the valve mechanism from the atrial ring, or even the endocardium of the atrium above, down to the papillary muscles below. The two cusps are thick, rigid, and often severely calcified; the size of the opening has already been mentioned, much larger than in pure mitral stenosis. When, however, we examine the chordæ tendineæ we find that the same primary and maximum adherence has occurred at the critical areas of insertion, but the commissures are very short and often extremely dense and frequently encroached upon by thick fibrous tissue occupying and bridging the peripheral groove between the under surface of the valve cusps and the ventricular muscle. This region may be occupied by exuberant calcium. The distance from the edge of the valve opening to the atrial ring is short (e.g. 0·75 cm. or less), but it must be emphasized that this is not because there has been only a minor peripheral degree of adherence of the cusps. The identification of the fusion in the critical areas contradicts this. The fused, thickened and densely matted chordæ are also seen to be shortened and the dense fibrosis extends down to involve the papillary muscles.

The reason for the larger orifice seems to be severe shortening and contracture of the cusps in all directions so that the central orifice, although diminished in size, is prevented from becoming smaller because of the radiating pull outwards of the fibrous tissue. Instead of the valve cusps

FIG. 17.—A valve from a severe case of mitral incompetence. Note the large, rigid, calcified orifice and the shortened cusps.

with a small orifice forming a funnel-shaped structure (Fig. 10) as in pure mitral stenosis, the shortened rigid cusps with the larger oval orifice present the typical " button-hole " appearance of the older morbid anatomists. It is necessary to repeat that in this type of valve we see the results of the most severe forms of valvitis.

Occasionally the cusps are not thick, opaque, leathery, and calcified but thin and fibrous, although still rigid and short. The orifice is some 2 cm. long, but the edges are thin and knife-like in their rigidity, instead of being thick and indurated. The commissures are similarly very short and it seems again as if the main process has been a peripheral fibrous contracture with resultant holding open of the central pathway of the fused shortened cusps.

Type 3. I have observed this form on three occasions at operation when clinically very severe mitral incompetence had been assessed: the striking feature is the large size of the orifice which is some 4 cm. × 2 cm., remaining open during systole when a wide and powerful regurgitant stream can be felt. In these cases the margins of the orifice were thin and fibrous, although quite rigid; the cusps thin, but fibrous and short. Both the left ventricle and the left atrium were very large and it was obvious that the atrioventricular ring was much larger in diameter than normal. The impression formed has been that there was not sufficient fibrous thickening to prevent dilatation of the atrial ring, thus the incompetence of the valve was further accentuated and a vicious circle set up.

In Type 2, in which there is a densely productive process, it seems as if the great rigidity of the whole valve mechanism prevents the extreme forms of incompetence developing as a result of progressive dilatation of the ring.

The Surgical Relief of Mitral Stenosis

It is essential to understand the morbid anatomical changes that can occur in the mitral valve mechanism, if satisfactory operations are to be performed upon the valve. It is not enough to look upon the problem as that of a fibrous diaphragm with a small oval aperture which only has to be made larger. Moreover, it should at once be made clear that although in many cases great improvement in valve function can be achieved by an operation and certainly stenosis can be considerably relieved, in some cases little or nothing can be done to lessen the stenosis or to improve or restore the valve-function by a direct operation on the diseased valve itself. In other words some cases are inoperable unless a means is found of substituting an alternative valve mechanism, possibly combined with partial excision of the damaged cusps.

It is also necessary to stress that the final assessment of the suitability of the valve for operative correction and the prognosis after operation can be made only when the valve is actually examined at operation. Even the presence of heavy calcification radiologically does not prove that the valve cannot be successfully operated upon. Two cases may appear to be identical clinically and yet at operation, one may have a simple stenosis which can be quickly corrected leaving thin supple cusps with a normal opening; the other may have a densely fibrous, rigid opening with short thick fused chordæ tendineæ which totally prevent more than a limited operative correction. In the first the prognosis should be good, in the second it must be uncertain.

Age is no guide. The outlook can still be good in a patient in the late forties or even over fifty, especially if the history is short; a valve with nice supple cusps may be found. In contrast a young patient may have uniformly dense, fibrous contracted valve cusps with thickened, fused, and grossly shortened chordæ tendineæ.

Fig. 18 shows the characteristic arrangement of the stenosed mitral valve viewed from above. The large aortic or anteromedial cusp and the smaller posterolateral cusp are well shown, together with the oblique axis of the valve orifice and the commissures. The fundamental step in valvotomy is, of course, restoration of the normal valve opening and preservation of the cusps by incising or splitting along the line of the fused commissures (Fig. 19).

In dividing the stenosed valve the surgeon must remember its essential funnel-shaped structure

FIG. 18.—Photograph of specimen of mitral stenosis to show the arrangement of the cusps and the oblique axis of the valve orifice.

and its convenient resolution into two parts, a distal transverse or horizontal central portion between the two areas of direct tendon insertion that contains the stenosed orifice, and a more proximal receding or oblique part on each side that extends from the areas of direct tendon insertion to the atrial ring (Fig. 20).

To split the central orifice as far as the two critical areas of tendon insertion on each side is

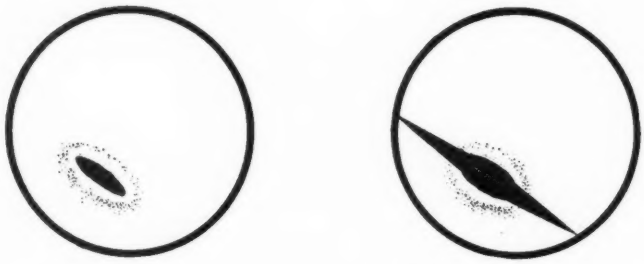


FIG. 19.—Diagram to show the directions in which incisions must be made along the line of the fused commissures if the stenosis is to be relieved in such a way as to restore the normal mechanism of the cusps and to avoid incompetence.

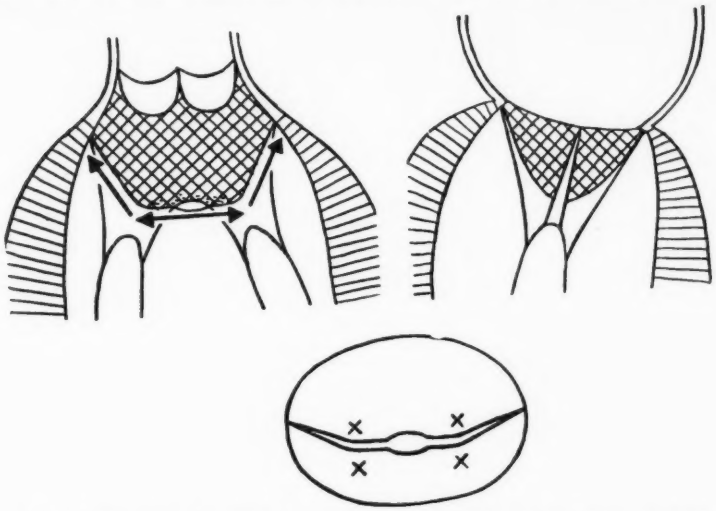


FIG. 20.—Diagram to show the essential mode of division of the stenosed mitral valve; the distal, central, portion is divided horizontally until the fused critical areas of tendon insertion are encountered and freed; the direction of division then becomes obliquely upwards along the sides of the mitral funnel.

usually simple. The resultant opening lies transversely. With the finger tip each main area of tendon insertion is investigated and if it is light and thin the fused valve can readily be split open along the line of the commissures, through the tendon zones, and then in an upward and outward direction (Fig. 20). The receding or ascending parts of the valve may be found almost as thin as tissue-paper.

As soon as the orifice has been enlarged sufficiently to permit the finger-tip to pass through without obstructing the opening completely, an attempt is made to palpate and assess the position and condition of the tendons and the papillary muscles. If the tendons are long, thin and separate, then one can feel confident of achieving an excellent result. Moreover, by identifying the papillary muscle, or muscles if there are two or if they are bifid, the exact line and direction of the commissures can be verified since the tendons spread out from the muscle equally to each cusp.

If firm resistance is encountered by the finger and the cusps do not split easily apart, the finger should be withdrawn and re-inserted bearing an appropriate valvotome. It should be a fundamental requirement of any valvotome that it does not permanently cover the flexor aspect of the terminal phalanx, for by so doing it prevents accurate palpation and localization. The one I favour (after having tried and rejected many designs) is a simple, thin-bladed, supple instrument (Fig. 21A) with which a cut can be made in exactly the right place. The blade slides up and down the finger in a groove in a ring which is worn around the finger base, so that it can be withdrawn to allow palpation and orientation with the finger tip and can then be advanced for the actual cutting (Fig. 21B and C). It can then be slid back again to allow the finger to feel and perhaps continue or complete the division. If the finger cannot complete the task the blade is slid forward once more to be used again.

Once the fibrous zone has been cut the finger may be made to pass between the chordæ tendineæ and the ventricular surface of the cusp; the tendons are often caught up on the under surface and can thus be separated. Thin chordæ tendineæ are sometimes felt actually adherent across the valve orifice so as to form a sort of lattice work in the opening, such an arrangement must be separated with the finger tip and not cut.

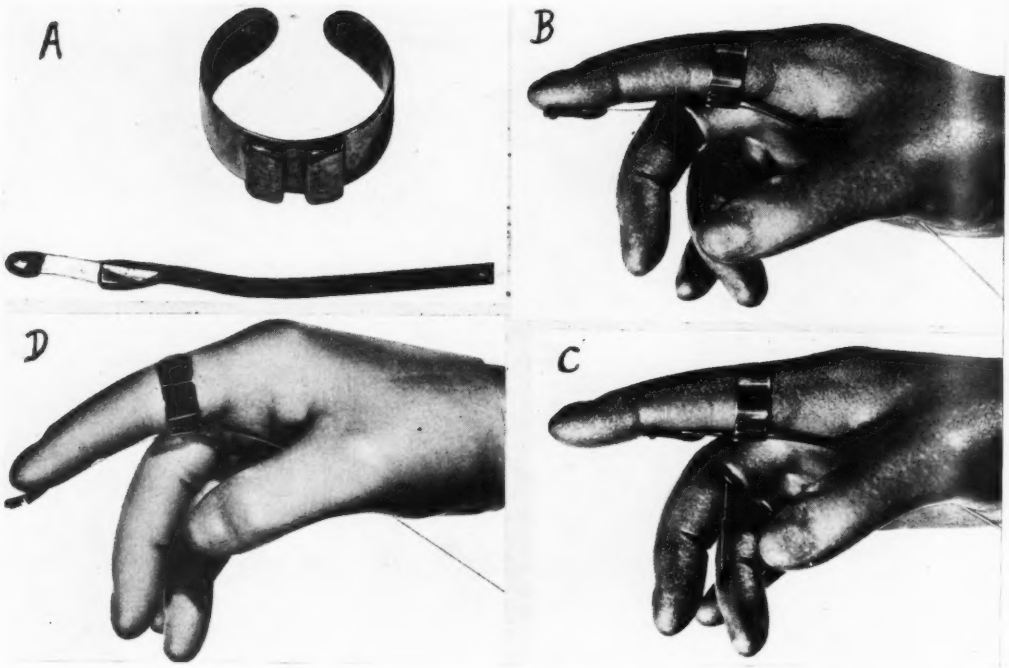


FIG. 21.—(A) Grooved finger ring and blade of valvotome. (B) and (C), To show the use of the valvotome with the blade for the lateral commissures. The instrument is introduced with the blade advanced; it is then retracted to allow the index finger to palpate the exact site for section; the blade is then advanced for the cut. In actual use another glove is worn with most of the index finger cut away. (D) The blade for the medial commissure has a cutting edge distally and along one edge; here again a second glove is worn over the first glove.

The fused valve cusps may be split easily right out to the A-V ring but the cusps may be prevented from opening because the chordæ tendineæ are fused. If light pressure is made downwards the tendons can usually be separated and the tethered cusps now open widely. Exploration of the chordæ tendineæ and papillary muscles is essential; in one case a localized cross fusion between two papillary muscles was recognized and separated.

For splitting the lateral commissure the finger is well flexed. For the medial commissure it is best to keep the finger perfectly straight and push gently but firmly along the line of the commissure with short movements from above downwards. If firm resistance is encountered a valvotome is used in which the cutting part is terminal and along one side (Fig. 21 D). This simple blade is very efficient for the medial commissure. The division of this commissure with certain instruments is often so awkward and difficult that it is frequently not attempted. Efforts have been made to cut it with the hand fully pronated, a manœuvre that is clumsy and unnecessary even if possible. There is no doubt that the medial commissure is best divided by cutting directly down on it. In this way what used to be a difficult manœuvre becomes quick and easy.

Fig. 20 illustrated the structure of the type of stenosed valve most favourable for division. If the simple, basic structure as detailed here is appreciated the steps of division can be followed easily. The distal transverse division is first made, then the two zones of direct tendon insertion are dealt with and then the ascending limbs of the two commissures are separated as far as the atrioventricular ring on each side. If the filigree pattern of thin separate chordæ tendineæ can be felt passing to their insertion into thin, pliable valve cups, it is fairly certain that the wide and well-functioning valve

orifice that has been restored (Fig. 22) is unlikely to contract down again unless the patient is unfortunate enough to suffer a further attack of rheumatic valvitis.

Not all valvotomies are as simple as this and the chief difficulty is usually encountered at the critical areas of tendon insertion. When tendons are fused and thickened so as to form large solid fibrous cords on each side of the small valve orifice (Fig. 11 and 12) a difficult situation is faced. In some it may be possible to cut or split the fused mass longitudinally so as to continue the division of the commissures and to allow the cusps to open. When, however, a thick, solid cord is found, as in Fig. 12, it is virtually impossible to carry the division of the valve through the firm barrier. Even if the cusps are split superficial to the fusion, the lateral parts cannot open since they will remain held by the cross fusion of the tendons and secondary fusion is bound to occur (Fig. 23). In these circumstances it may be necessary to be content with enlargement of the small central pathway only as far as the two critical areas. Such an opening can never be more than some 1·5 cm.–2 cm. and is almost bound sooner or later to undergo considerable secondary contracture.

The question is often asked whether recurrence of stenosis is likely after mitral valvotomy. The answer is that, barring further rheumatic valvitis, recurrence is unlikely provided the free movement of the valve cusps is completely restored by ensuring division and separation of the critical areas of tendon insertion. If this is not done, then recurrence is likely. Even if one complete commissure is divided and the corresponding area of direct tendon insertion freed (Fig. 24) a lasting good result should be obtained.

FIG. 22.—Photograph of mitral valve after valvotomy to show the complete restoration of the opening and the reformation of the two functioning flaps. The small size of the original orifice can be seen in the margin of the posterolateral flap.

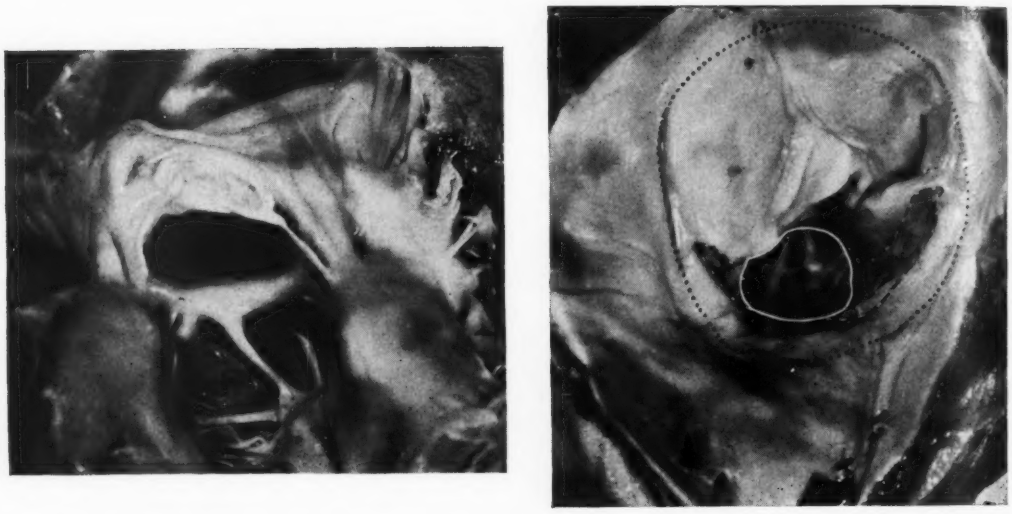
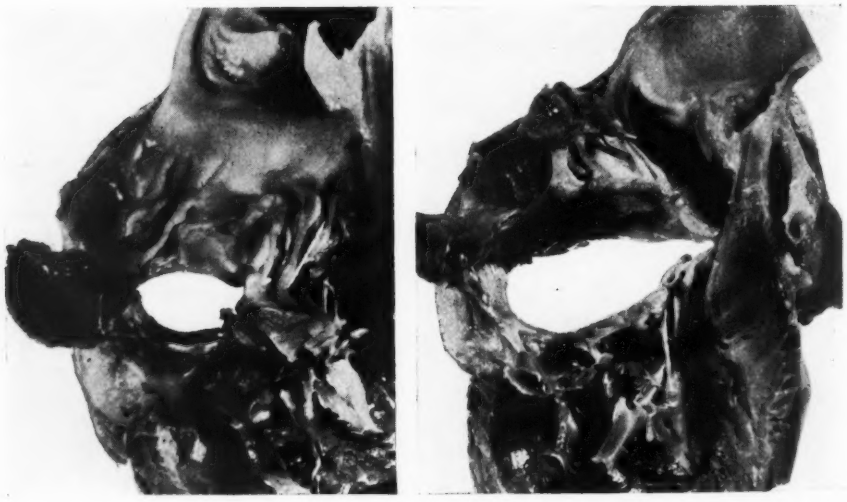


FIG. 23.—Photograph of specimen, two years after valvotomy, to show the mechanism of refusion of the cusps. The commissures of the valve cusps had been completely divided as far out as the atrioventricular ring; the chordæ tendineæ were, however, so solidly fused, that they could not be separated; secondary refusion of the commissures was, therefore, inevitable, although a reasonably good central pathway remained. Sudden death occurred after quinidine therapy. The clinical result had been excellent.



A B

FIG. 24.—Photograph of a specimen viewed from below, of mitral stenosis in which, at operation, only one commissure was completely cut. In (A) the chordæ tendineæ of the lateral commissure are placed together as they were before valvotomy; in (B) the chordæ tendineæ of the lateral commissure have been separated to show how the valve cusps are liberated and allowed to open freely. The medial commissure remains fused and this part of the valve cusp, therefore, cannot open.

If a solid barrier of fused tendons is encountered and the division of the valve is carried round in front of or behind it, incompetence is bound to follow. If the cut passes in front, the aortic cusp will be deprived of its support and the incompetence will be severe and possibly fatal. If the cut passes behind, only the posterolateral cusp will be affected and the regurgitation will be less significant.

The Surgical Relief of Mitral Regurgitation

The small, rigid, stenosed orifice through which a small amount of regurgitation occurs presents no real problem, for the division of the fused cusps and tendons automatically corrects the regurgitation; which in any case is of an insignificant degree.

The real problem begins when the orifice is not a very small one, but is between 1 cm. and 2 cm. long and from 0·5 cm. to 1 cm. wide, and is rigid, perhaps calcified, and flanked by short, rigid, very fibrous and thickened cusps which form, not a funnel, but an almost flat diaphragm with a button-hole orifice. The chief reason for the valve's incompetence is the shortness of the cusps which prevents overlap or free co-aptation of their edges. The effect of enlarging the orifice by dividing the commissures, an act that in any case is limited by the shortness of the commissures, is in general to make the incompetence worse. The edges of the orifice remain rigid and the cusps are not only too short and stiff to overlap but, from their fibrous nature, may even retract. In only one case have I observed a different action; this was in the case of a woman, aged 54, with a rigid, semi-calcified incompetent orifice. The lateral commissure was almost completely calcified; as the medial commissure was cut the regurgitant stream, which the finger was sensible of, ceased abruptly as if the division of the commissure had allowed the two cusps so to readjust themselves as to become more efficient.

In general it is useless to expect improvement by performing valvotomy on an incompetent rigid valve with short thick cusps and an orifice some 2 cm. long. The decision that must be made is whether some plastic procedure should be used to reinforce or correct the valve's incompetence. There is no doubt that some such procedure is urgently needed because it is a serious thing to operate on a case of mitral valve disease and close the chest again without improving the heart's action; the result is almost certainly the death of the patient. The only reason why thoracotomy and cardiotomy is possible on severely ill patients with mitral stenosis is that the valvotomy immediately improves the heart's action. If a patient submits to such an operation then he should be given the chance of some real improvement.

In the third type of mitral incompetence, that in which the orifice is very large, the atrial ring very dilated, the cusps short and the degree of regurgitation severe, the problem is even more difficult. The powerful left ventricle and the large valvular defect produce a massive reflux, the control of which is a severe test for any plastic procedure.

Unfortunately at present no reasonably safe and successful procedure is available; the method of introducing pericardial flaps into the ventricle has proved, so far, disappointing and dangerous. Although the present methods have proved disappointing, it is desirable to consider more critically the anatomical problems involved so that an improved method may be evolved with some degree of accuracy.

The insertion of a pericardial flap through two openings, so that it may form a flapper valve to close the incompetent orifice, has certain grave defects in its usual method of application. In order that such a flap should function efficiently it must be disposed at right angles to the long axis of the valve opening (Fig. 25). It could not be parallel to this axis, for the papillary muscles and their tendons are in the way. Fig. 25 shows, diagrammatically but accurately, the disposition of the mitral orifice (cf. Fig. 18, a photograph from an actual specimen). The line A–A indicates the position that must be occupied by a pericardial flap if it is to lie transversely to the long axis of the valve orifice. It will be seen that, anteriorly, it must traverse the outflow track of the left ventricle, the septum, and the outflow track of the right ventricle. Clearly this is impossible.

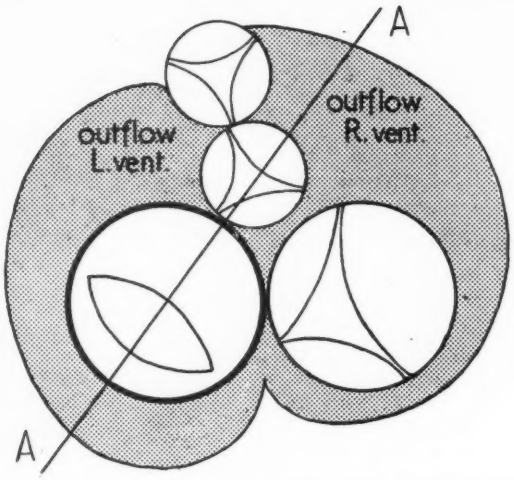


FIG. 25.—Diagram to show the basic anatomy of mitral incompetence. The line A–A indicates that if a pericadial flap with two opposing sites of fixation is to be used in such a way that it is efficient it must lie at right angles to the axis of the valve orifice and inevitably, therefore, it must traverse, in front, the outflow tract of the left ventricle, the septum and the outflow tract of the right ventricle. To avoid these structures it must lie at a much less efficient angle to the optimum line A–A.

If the septum and the right ventricle are to be avoided the anterior fixation must be at an angle considerably less than 90 degrees to the long axis of the valve orifice and in fact forming, not the diameter of the circle of the valve ring, but a chord. Its efficiency in controlling valvular incompetence diminishes as the angle diminishes. Moreover, it is by no means certain that such an ill-disposed flap will be flung against the incompetent mitral orifice in systole. It may just as well, or even more likely, be shot into the outflow channel of the ventricle.

The incompetence is due, fundamentally, to the fact that the two cusps are too short to meet and overlap so as to give mutual support. The most logical method of correction of the disability would seem to be lengthening one or both cusps so that they can reach and overlap. The anterolateral or aortic cusp does not lend itself to such a procedure, seeing that its ventricular surface is directly related to the outflow channel. We must, therefore, turn to the posterolateral cusp which lies essentially in the inflow portion of the ventricle. If this cusp could be either lengthened or reinforced by a flap or some other structure introduced immediately beneath it, its function should be restored (Fig. 26). Thus any material used to correct incompetence should be inserted so that it is hinged posterolaterally, as shown in Fig. 26. This might be a two-pedicled flap of, e.g. pericardium, introduced from outside the ventricle; the disadvantage of this method is that the access to the relevant part of the ventricle is difficult and awkward. An alternative method is the introduction of a flap from within the heart, sutures being passed through the wall of the ventricle from within outwards to guide the flap into place and to fix it securely. Such a flap can be inserted via the left auricular appendage. This method has the same drawback of difficult access to the correct sites high enough and far enough back on the left ventricle. A flap successfully introduced into position below and re-inforcing the posterolateral cusp must inevitably be flung against or across the valve orifice in systole; it cannot be diverted into the outflow channel.

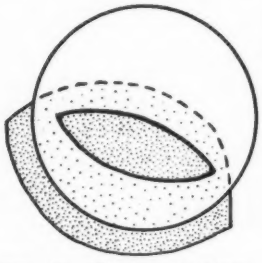


FIG. 26.—Diagram to show suggested correct mode of application of a re-inforcing flap to control mitral regurgitation by extending the surface of contact of the posterolateral cusp.

I have used each of these methods in trial cases, but so far without success. This analysis of the relevant anatomical features, or what would appear to be the relevant features, is put forward, not because it has been proved correct in practice, but because it appears to be sound in theory. It may serve to help in the planning and execution of some alternative form of mitral valvoplasty to correct incompetence.

REFERENCES

Bourne, G. (1952). *Brit. med. J.*, **1**, 896.
Brock, R. C. (1950). *Guy's Hosp. Rep.*, **99**, 236.
Lutembacher, R. (1950). *Le Rétrécissement Mitral.* Paris.
McMillan, I. K. R., Daley, R., and Matthews, M. B. (1952). *Brit. Heart J.*, **14**, 42.
Magarey, F. R. (1951). *Brit. med. J.*, **1**, 856.
Quain's Anatomy (1929). 11th edit., Vol. IV, The Heart. London.
Rusted, I. E., Scheifley, C. H., Edwards, J. E., and Kirklin, J. W. (1951). *Proc. Mayo Clin.*, **26**, 297.
Smith, J. C. (1950). *Circulation*, **1**, 766.
Sokoloff, L., Elster, S. K., and Righthand, N. (1950). *Circulation*, **1**, 782.

THE ANOXÆMIC TEST FOR CORONARY INSUFFICIENCY

BY

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Physicians have long felt the need for some confirmatory test when coronary insufficiency is suspected but cannot be proved, that is to say when physical examination and resting electrocardiograms are normal. The principal problem lies in the interpretation of pain in the chest. Such a test is, of course, unnecessary apart from academic interest when the diagnosis is clear. Assistance would be particularly welcome when the history is not quite characteristic and especially perhaps in the younger age groups. Preferably too, a negative result would exclude angina as the basis for atypical pain. An objective test is much more satisfactory than a clinical impression. To this end a number of procedures have been devised and include adrenaline, pitressin, exercise and anoxæmic tests. The assessment is made on the electrocardiographic changes observed.

TESTS THAT HAVE BEEN USED

The Adrenaline Test. Levine (1930) first recommended the use of adrenaline. Typical pain was reproduced in all those suspected of having angina but in none of the controls. The T waves showed an increase in height in the patients and a tendency to decrease in the controls. No changes in the S–T segment were observed. However, Katz *et al.* (1932) concluded that the results were too unreliable for clinical purposes and at least one group has found the test dangerous (Cottrel and Wood, 1931). It seems to have been little used since.

The Pitressin Test. Ruskin (1947) suggested the use of pitressin which is a powerful constrictor of the coronary vessels. He found good correlation with the exercise test. A positive result was taken to be a change from an upright T wave in Leads I, II, III or IV to a flat or negative one and depression of the S–T segment totalling 3 mm. or more in Leads I, II, III or IV. There were no positive findings in normal controls and a negative test was not taken to exclude the presence of angina pectoris. However, he considered the potential risks of the test were such as to preclude its general use.

The Exercise Test. This is the most familar test and bears the merit of simplicity. It will not be discussed in detail here. The technique has varied a good deal between different observers as have criteria of abnormality. Either the patient can be given a definite amount of exertion standardized for his age, sex and weight as recommended by Master (1942, 1944) or else he can be exercised until pain develops or he becomes unduly breathless (Riseman, Waller, and Brown 1940). Records are taken before, immediately after and a few minutes after the exertion and the characteristic changes in the S–T segment and T wave, which are similar to those observed in the anoxæmic test, accurately measured. The circumstances under which the pain is naturally experienced are closely reproduced; but there are disadvantages. Electrocardiograms cannot be recorded until after the

exertion is over, and not all patients can take sufficient exercise; moreover, though the test can be stopped should any untoward symptoms ensue, its effects may not be rapidly reversible. The deviations from normal are relatively slight and must be measured in fractions of a millimetre. Moreover, measurement is often rendered difficult by the muscle tremor and tachycardia associated with exercise. These factors militate against accuracy. However, the purpose of this paper is not to decry the exercise test, the value of which is established.

The Anoxæmic Test

The anoxæmic test would appear to offer certain advantages. A mixture containing 10 per cent oxygen and 90 per cent nitrogen is administered through an anæsthetic mask. The patient is resting and, if confidence has been gained, relaxed. Records are easily made throughout the test and should pain or any other untoward symptoms occur, 100 per cent oxygen is always immediately to hand.

Greene and Gilbert (1921) were the first to study the effects of anoxæmia on the electrocardiogram in humans and Resnick in animals (1925). Ward and Wright (1929) showed that similar changes from breathing pure nitrous oxide were due to the anoxæmia produced.

The work of Kountz and Gruber (1929) was followed by their suggestion that induced anoxia might form the basis for a clinical test for coronary insufficiency and this was subsequently introduced by Rothschild and Kissin (1933). They noted depression of the S–T segments and T waves in patients with angina. The severe anoxæmia ultimately resulting from the re-breathing technique, which all early workers used, produced similar changes of lesser degree in healthy controls. They also found that such changes might be recorded during spontaneous attacks of angina pectoris. Katz's group (1934) investigated the possibilities of this test and made essentially similar observations but concluded that the results were too variable and the potential hazards too great for clinical work. Larsen in Copenhagen (1938) recommended the administration of a constant mixture containing 9 per cent oxygen in nitrogen, without rebreathing, to patients with suspected angina. He noted the lack of any constant relationship between the occurrence of pain in the chest and the electrocardiographic changes during the test. The degree of S–T deviation and T wave depression was measured and the test advocated as a practical clinical procedure. Levy (1938, 1939, 1941 *a* and *b*, 1946) has been closely associated with the development of the anoxæmia test for coronary insufficiency and has gradually evolved a standardized procedure with definite criteria of abnormality that have been accepted by the majority of subsequent workers.

The problem has been studied by numerous groups of workers since this time and general agreement reached on the type of change produced in healthy subjects and in patients known or suspected to have, coronary artery disease. Opinions have differed somewhat as to the value of the test in practice and on its relative merits compared with the exercise test but on the whole reports have been favourable. Levy and his co-workers are quite convinced and remain enthusiastic supporters of the test. Their studies have now continued for over ten years. Extensive experience has also been gained in the Mayo Clinic by Burchell's group (1948). They consider that the test has been established as having a small but useful role in the study of coronary disease. In Nylin's clinic in Stockholm (1942, 1943) the problem has also been thoroughly investigated and continues to be studied there by Biörck (1946 *a* and *b*). Some 900 tests are made each year. Malmström (1947) also makes extensive use of the test in Sweden. Support has also come from Weintraub and Bishop in Arkansas (1947) and by Stewart's group at the New York Hospital (1948).

Riseman *et al.* (1940) doubt whether there are sufficient differences between normal subjects and patients to avoid errors with either the anoxic or exercise tests. Adverse criticism from Burnett's group in Colorado (1942) was counter-attacked by Patterson *et al.* (1942), largely on the grounds that their tests were carried out at an altitude of 6000 feet where a 10 per cent oxygen mixture is equivalent to 8 per cent at sea level. This involves a more severe test than the standard procedure and hence the results are not strictly comparable with those of other authors. Only one paper has

come from Great Britain; that by Evans and Bourne (1940). They studied patients with definite angina rather than problem cases and gave the nitrogen mixture for rather a short time. Significant changes occurred in about half of their patients with angina who had a normal resting electrocardiogram. A very useful study of large numbers of normal people in different age groups was made by Burnett *et al.* (1942). They could find no correlation between the number of positive tests and increasing age such as might have been expected.

Master (1944) is satisfied that the exercise test is more reliable. Stewart *et al.* (1948), Biörck (1946) and Riseman *et al.* (1940) prefer the anoxic test and Grossman's group (1949) considers that any difference between the two is probably slight. Evans and Bourne (1940) decided the exercise test held some advantages. We are of the opinion that both tests have a part to play in difficult cases but that the anoxæmic test is preferable in the first instance.

The results of the anoxæmic test are empirical in that they are based on the comparison between the changes found in healthy persons and those known to be suffering from coronary artery disease. Varying attention has been given to factors other than anoxæmia or ischæmia which may influence the S–T segment and T waves of the electrocardiogram. Very often the test has been carried out quite unnecessarily in that the diagnosis was not really in doubt. Clearly there has been some difference of opinion as to the value and validity of the test. Owing to the need felt for assistance in certain cases we thought it would be worth while to re-evaluate it in the light of personal experience. Attention was confined to patients who presented a definite clinical problem, and the results were analysed to see how far clinical judgment was affected by the results of the test. Problem cases include those in which pain is atypical in situation, duration, quality or relationship to effort or in reponse to glyceryl trinitrate and those in which the functional factor is so predominant as to make differentiation between cardiac and non-cardiac symptoms impossible.

In this paper the effects of the anoxæmic test have been considered to be related to coronary insufficiency. However, others have used the test to assess myocardial insufficiency per se, i.e. in patients believed to have normal coronary arteries. Mannheimer (1946, 1948) is convinced of the value of this procedure as a test of myocardial insufficiency in children. He uses it almost as a routine investigation in cases of myocarditis and of acyanotic congenital heart disease. Master (1944) studied a group of adults with valvular disease and considered the test useful for assessing the degree of anoxæmia of the heart muscle during exercise. The first part of what follows deals with the practical aspects and the second with the theoretical side of the problem.

Technique and Criteria

Cylinders containing the oxygen–nitrogen mixture can be obtained from the British Oxygen Company and a large one with enough gas for a dozen patients costs less than five shillings. An anæsthetist was usually asked to administer the mixture not because an anæsthetist is really necessary but because it enables the physician's attention to be given entirely to the patient. Great care was taken to explain the test to the patient to ensure that confidence had been fully gained. A standard Boyle's anæsthetic machine proved satisfactory and the mixture was given through an ordinary mask at a rate of about ten litres per minute. It has usually been recommended that the gas should be given for twenty minutes but an analysis of our cases showed that ten minutes was quite sufficient and actually the cardiographic changes may regress after this time owing presumably to compensatory effects. Indeed, we have found that changes are almost always present after five minutes. We have had the advantage of using an Elmquist Triplex 4-galvanometer machine. A direct writing machine would be an obvious advantage. Records were taken after five and after ten minutes, or earlier if there were any manifestation of distress, in which case the test was immediately discontinued. 100 per cent oxygen was given for one minute at the completion of the procedure and further records taken five minutes later. If the results were negative and angina suspected, an exercise test was sometimes carried out using the same leads.

In 1942 Levy published his revised criteria which indicated that the test should be considered positive under any of the following conditions.

1. The arithmetical sum of the S–T depressions in leads I, II, III, and IV is greater than the control by 3 mm. or more.
2. Reversal of T wave in lead I associated with S–T depression in that lead of 1 mm. or more.
3. Complete inversion of the T wave in lead IV.

The above criteria were generally accepted and have been used by most workers since. They were re-assessed and re-affirmed by Weintraub and Bishop in 1947. However, Burnett (1942) on the basis of 125 tests on normal subjects had suggested that the third criterion was unreliable as 22 normal subjects showed reversal of T in CR4. These results were criticized by Patterson *et al.* (1942) on the grounds of the high altitude at which the tests were carried out, as mentioned above, and the possibility that many of the cases were in fact not normal. For reasons given below we are of the opinion that this third criterion is, in fact, unreliable. Criteria of abnormality should be strict because the object of these tests is not to obtain the maximum number of positives but to obtain convincing help in difficult cases.

Subjective Test. Even in the absence of cardiographic changes, this test might be considered positive if the patient experienced retrosternal pain. This, of course, throws the responsibility back on to the physician who has to interpret the subjective sensations. An experienced observer should be capable of assessing the value of such a positive test. If pain resembling angina and similar to that naturally experienced comes on with the development of anoxæmia and responds to oxygen, administered to the patient without his knowledge, then even in the absence of concomitant electrocardiographic changes the test may reasonably be considered a positive one. We have been convinced of the value of such assistance on occasion. In the anoxæmic test, pain and the electrocardiographic changes may occur quite independently.

Reactions. Naturally the patients become cyanosed. Routine arterial oxygen saturations have not been estimated because it has been established that the oxygen saturation varies considerably between different subjects breathing the same mixture (Dripps and Comroe, 1947; Penneys and Thomas, 1948; Stewart *et al.*, 1948). Moreover, neither the occurrence of pain nor electrocardiographic changes are closely related to a certain critical level of oxygen saturation (Levy *et al.*, 1938; Stewart *et al.*, 1948). However, it is a reasonable suggestion that a constant level should be maintained with the help of an oximeter (75 per cent saturation).

The effects of anoxia on healthy persons are familiar to physiologists. Even loss of consciousness is known not to be dangerous if observed early. The few reactions which we have experienced and most of those previously reported can be explained on the basis of anxiety or occasionally cerebral anoxia. These include such symptoms as headache, dizziness, tingling, restlessness, and respiratory discomfort. Serious reactions have not been reported except in the early days in the United States when a few patients with recent infarction or cardiac failure were tested. However, a few workers have reported vaso-vagal attacks characterized by fall of blood pressure and slowing of the heart with pallor, sweating and occasional syncope. Such episodes must be very uncommon and respond to the administration of oxygen. Properly conducted, the anoxæmic test is not dangerous; reactions other than minor discomfort were only experienced in two of our patients; momentary loss of consciousness and twitching occurred, with rapid recovery on turning off the nitrogen and giving pure oxygen. The patients were unaware of the incident and there were no after-effects. Both of them were subsequently found to be anæmic. In each case the hæmoglobin was about 65 per cent. This is clearly an important point which should have been observed and taken into account. We have had no reactions in the last three years.

Controls

Although control tests have been carried out by numerous workers it was necessary to obtain our own experience and become familiar with all aspects of the procedure and to confirm the normal range for our apparatus and technique. It was not, however, considered necessary to undertake large numbers of controls in patients of all ages as this work has been thoroughly done before (Burnett *et al.*, 1942).

The tests were all done on healthy volunteers. They consisted of members of the staff, registrars, housemen, and students. Twenty out of the 21 control tests were considered normal—the deviations from the resting records being relatively slight and within the accepted range of normal. Fig. 1 serves to demonstrate the type of record taken. Leads I, II, III, and IV were recorded simultaneously and hence it sometimes happens that a tall R wave runs into the QRS complex immediately above though this does not affect the subsequent measurements. S–T segment depressions have to be added together so that an elevation at rest (as in Lead II here) must be allowed for. The isoelectric line was taken from the P–Q segment and deviations were measured in millimetres. One case deserves special mention. A healthy male, aged 40, was able to undertake strenuous exercise without pain or dyspnœa, yet total S–T depression in the anoxæmic test just amounted to 3 mm. (Fig. 2). This is at the upper limit of the accepted normal range in that total S–T depression of 3 mm. or more is taken to mean a pathological test. This serves as a reminder, which will be referred to later, that in any such test with an arbitrary border line between normal and abnormal, there will inevitably be some cases near the line which require caution in interpretation. In this instance there has been no adverse development during an observation period of three years.

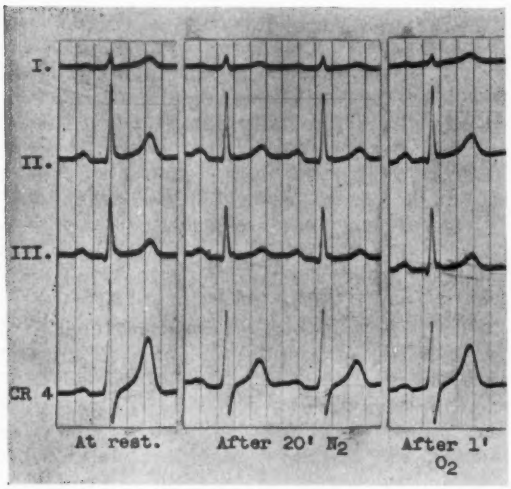


Fig. 1.—Control subject. Negative anoxæmic test.

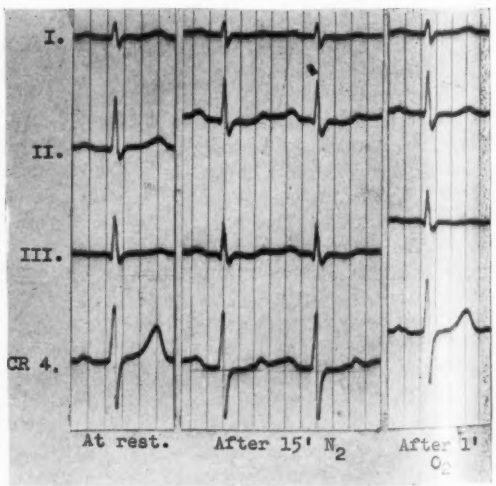


Fig. 2.—Control subject. Total S–T depression just 3 mm. Borderline test (see text).

Patients

The findings in our cases are shown in detail in Table I and summarized in Table II. Of 30 patients examined, 14 developed abnormal cardiographic changes and 11 experienced anginal pain. In some instances objective and subjective evidence was obtained from the same individual.

From this table it will be seen that 29 out of the 30 patients have been followed up and most of them for 16–32 months. During this time it has been possible to reach a confident diagnosis on

TABLE I

DETAILS OF RESULTS IN 30 CASES

Case	Sex	Objective test	Subjective test	Follow-up in months	Clinical assessment at end of follow-up
			Patients with normal resting cardiogram		
			Group (a)		
1	M	Pos.	Neg.	32	A.P.
2	M	Neg.	Neg.	31	A.P.
3	M	Pos.	Pos.	27	A.P.
4	F	Neg.	Neg.	27	No A.P.
5	M	Pos.	Pos.	24	M.I. in 11th month—recovered
6	M	Neg.	Pos.	20	Test repeated at 12th month. Pain reproduced but no E.C.G. changes. Again repeated 4 months later—positive objective and subjective test. Subsequently developed M.I.
7	M	Pos.	Pos.	4	Died. M.I.
8	F	Neg.	Neg.	19	A.P. after 19 months
9	M	Neg.	Neg.	—	No follow-up available
			Group (b)		
10	F	Neg.	Neg.	28	No A.P.
11	F	Pos.	Pos.	30	A.P. Test repeated at 24th month—again positive
12	F	Pos.	Pos.	30	A.P.
13	F	Neg.	Neg.	29	A.P. probable
14	F	Neg.	Neg.	29	No A.P.
15	M	Pos.	Pos.	28	A.P.
16	F	Pos.	Neg.	24	A.P.
17	F	Neg.	Neg.	23	No A.P.
18	M	Neg.	Neg.	16	No A.P.
19	F	Neg.	Neg.	19	No A.P.
20	F	Neg.	Pos.	18	A.P.
21	M	Pos.	Pos.	16	A.P. Test repeated at 7th month—again positive
22	F	Pos.	Neg.	10	A.P.
23	M	Neg.	Neg.	8	No. A.P.
24	F	Pos.	Neg.	6	A.P.
25	F	Pos.	Neg.	6	A.P.
			Patients with abnormal resting cardiogram		
26	M	Neg.	Neg.	29	M.I. in 18th month—recovered
27	M	Neg.	Neg.	28	No A.P. Believed to have neurotic pain
28	F	Pos.	Pos.	24	A.P.
29	M	Neg.	Neg.	20	Died. M.I. probable
30	M	Pos.	Pos.	1	Died. No P.M.

A.P. = Angina pectoris. M.I. = Myocardial infarction. (*a*) see text. (*b*) see text.

clinical grounds and it will be seen that the results of the anoxæmic test, carried out when the patient was first seen, was subsequently confirmed in 23 of the 30 patients. Six patients in whom a negative test was obtained subsequently developed angina of effort or a myocardial infarction. This suggests that no errors were made on the positive side but that a negative test does not exclude coronary disease.

TABLE II

SUMMARY OF RESULTS IN 30 CASES AND 21 CONTROLS

		*OBJECTIVE TEST**	
		Positive	*Negative*
Controls	21	1	20
Patients	30	14	16

		SUBJECTIVE TEST (ANGINAL PAIN)	
		Positive	*Negative*
Controls	21	0	21
Patients	30	11 (9 E.C. positive) (2 E.C. negative)	19

*Cardiographic criteria of Levy (see text)

In 25 of these 30 cases, resting electrocardiograms were quite normal Standard limb leads and at least three (usually six) chest leads were recorded In none of the cases presented was the diagnosis considered certain. Each had atypical features. The degree of clinical doubt varied from case to case. Objective evidence was preferred to a complaint of pain and attention was only paid to unequivocal changes. On the whole the results of the anoxæmic tests fitted in with our clinical impressions and positive results were obtained when most expected. Nevertheless the information was of definite value in these positive cases in that a firm diagnosis could be made. In some of our patients considerable differences of opinion had been expressed. For purpose of analysis the patients should really be divided into two groups. Group (*a*) Table I consisted of cases in whom angina was really suspected though some unusual feature was present and all other methods of examination were negative. It was in this group in particular that we gained our initial experience. In this Group (*a*) 4 out of 9 patients developed abnormal cardiograms and 3 of these 4 also experienced anginal pain. One patient developed pain but no graphic changes. Group (*b*) consisted of more difficult problem cases; 8 out of 16 patients developed abnormal records and 4 of these 8 also experienced pain. One patient developed pain but no cardiographic changes.

It is doubtful how much significance should be attached to negative results. A patient with a negative test may subsequently develop myocardial infarction. This happened to 2 of our patients, one 18 and one 20 months later. It may well be that a negative test does suggest that the symptoms complained of at the time are not of ischæmic origin. However, caution is obviously required in this group and a dogmatic opinion cannot be reached. A negative test can give no more than guarded reassurance to the physician. Clearly there is a varying balance between the factors responsible for the accumulation of metabolites or whatever is the ultimate mechanism in the production of pain and the increased coronary blood flow resulting from anoxæmia particularly as regards the capacity of an anastomotic circulation to nourish the pain-producing area. In addition to the direct effects of anoxæmia on the heart, there must be considered the indirect effects on the cardiovascular system from stimulation of the respiratory and nervous systems, resulting in variations of ventilation, heart rate, blood pressure, and the work done by the heart. Moreover, as referred to above, the arterial oxygen saturation varies considerably in different individuals and from time to time in the same individual breathing a constant low oxygen mixture.

Five of the 30 patients had abnormal records at rest and a history suggesting past myocardial infarction. Patients with recent infarction, of course, were not examined. Nevertheless the pain complained of was not characteristic and difficult to interpret. Patients in this group were usually neurotic or at least an associated functional factor was thought to be predominant. In 2 of these 5 cases, a positive objective result was obtained—that is to say ischæmic changes were superimposed on the previous abnormality and both of them developed angina during the test. The other 3 tests in this group of 5 cases were negative. We feel that valuable information was also obtained in these two positive cases. In spite of the presence of organic heart disease it had been considered that the pain was probably due to anxiety. Four cases will now be considered by way of illustration.

Case 21. A soldier, aged 36. Two years history of epigastric pain related to exertion, especially after meals. Long periods of remission. Ischæmic pain suspected but atypical features present. In view of relatively young age and the fact that he was a regular army officer a definite diagnosis was particularly desirable. Clinical examination, X-ray and cardiograms negative. Barium meal normal. No hiatus hernia. Positive anoxæmic test (total S–T depression=6½ mm. Fig. 3; Case 21). Follow-up confirmed diagnosis.

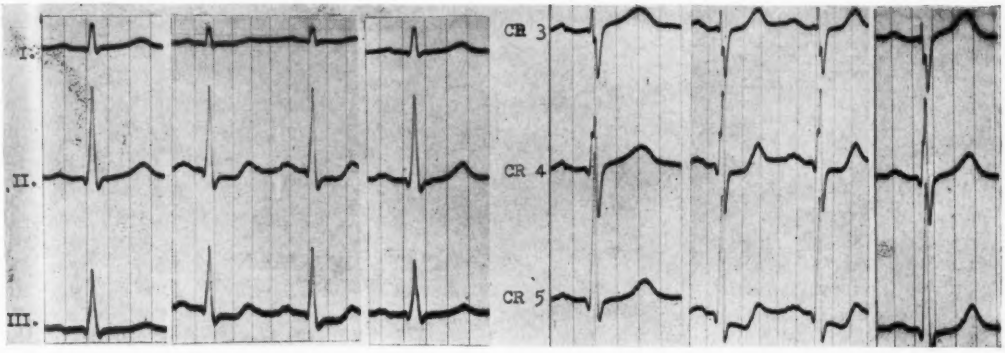


FIG. 3.—Case 21. Positive anoxæmic test. Total S–T depression 6½ mm.

Case 12. A woman, aged 55. Rheumatic aortic incompetence. Retrosternal and left mammary pain not closely related to exertion and with varying characteristics. An exceedingly neurotic woman, whose pain was difficult to assess. Resting cardiograms within normal range. Positive anoxæmic test (total S–T depression=7 mm. Fig. 4; Case 12).

Case 30. A man, aged 50. Myocardial infarction two years previously followed by left lower chest pain related to walking but unrelated to other heavy physical exertion. Pain also had other atypical features.

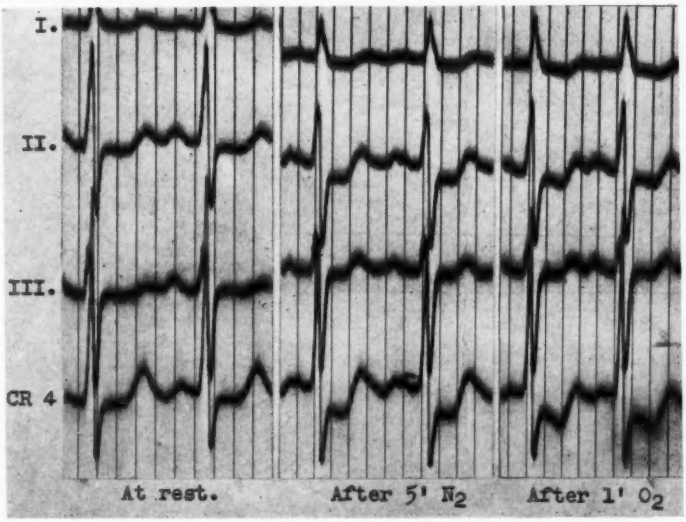


FIG. 4.—Case 12. Positive anoxæmic test. Total S–T depression 7 mm.

Clinical and X-ray examinations negative. Resting cardiograms showed healed posterior myocardial infarction. Positive anoxic test (total S–T depression=5 mm. Fig. 5; Case 30) indicating that his pain was still due to myocardial ischæmia. Died suddenly two months later. No post mortem.

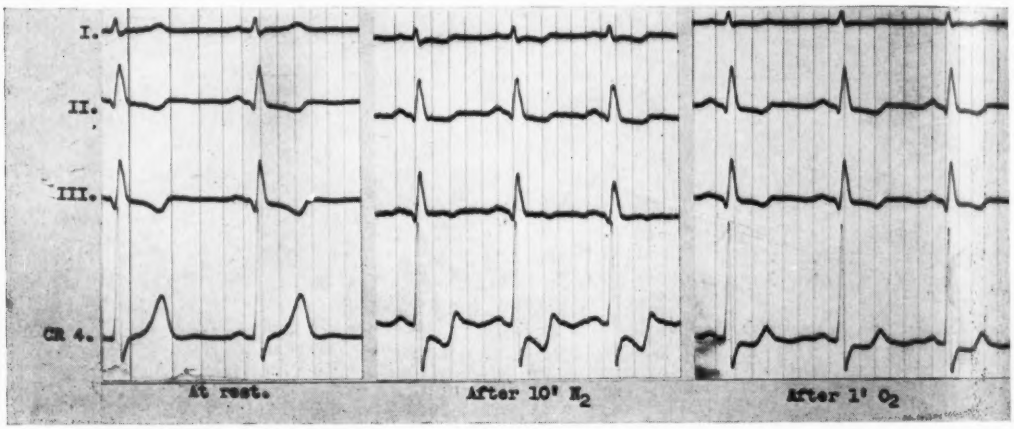
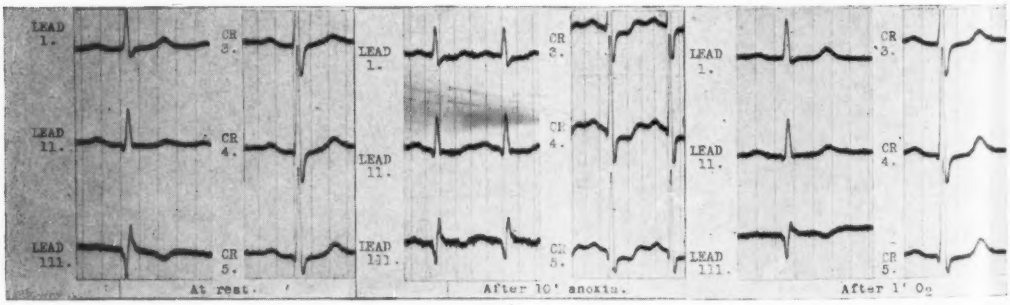
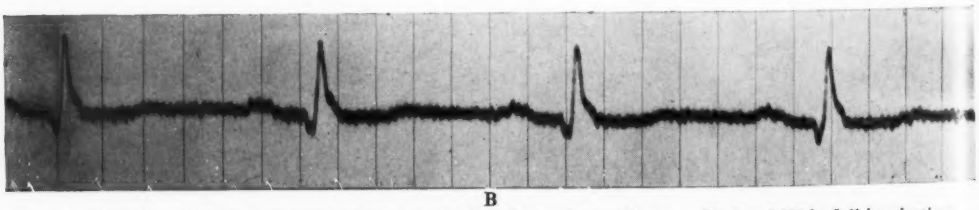


FIG 5.—Case 30. Positive anoxæmic test: total S–T depression 5 mm.

Case 25. A woman, aged 68, gave a twelve-month history of retrosternal burning pain frequently coming on at rest in bed, but sometimes related to exertion. Not immediately relieved by trinitrin. Hiatus hernia was suspected, but excluded. Physical examination and screening of the heart were negative, apart from the finding of obesity and a high diaphragm. Resting cardiograms showed only a $Q_{III}T_{III}$ pattern which disappeared on deep inspiration and hence was not considered to signify myocardial infarction. Anoxæmic test was positive and confirmed the diagnosis (total S–T depression = 4½ mm) (Fig. 6).



A



B

FIG. 6.—Case 25. (A) Positive anoxæmic test: total S–T depression = 4½ mm. (B) Lead III in full inspiration.

Discussion of Results

What then is the potential value of the anoxæmic test? First, to try and confirm that a suspicious pain is in fact based on ischæmic heart disease. Secondly, to try to exclude angina pectoris as the cause of an atypical chest pain. Thirdly, to try to assess the degree of recovery following previous myocardial infarction. Fourthly, to help in deciding the fitness of a patient for a surgical operation and especially the anæsthetic. Fifthly, there is a possibility of assistance in assessing the value of drugs on the coronary circulation.

Information of some value and considerable interest has been obtained in about one-half of our cases. The series has been analysed but is hardly worthy of statistical presentation.

Instead of large numbers called from far and wide to make a big series we have studied, as carefully as possible, individual patients whom we knew well, as opportunity offered. Naturally such cases are not so very common. Each presented a real clinical problem and the information obtained was used in conjunction with the other evidence to come to a more definite opinion. On occasion we have used the test when some operation, not of an essential nature but yet advisable if there is no undue risk, is under consideration. A negative result has been taken as suggesting fitness for general anæsthesia. The anoxæmic test is not a reliable guide to prognosis.

With proper selection of patients and due precautions, the dangers of the test are minimal. It can be carried out in any hospital with average facilities. There is neither need nor justification for this procedure when the diagnosis has already been established or where no reasonable doubt exists. No patient should be submitted to it before a full series of electrocardiograms have been taken and examined; that is to say at least 9 leads consisting of 3 standard (or unipolar) limb leads and 6–7 chest leads. On a number of occasions when four leads have been normal we have found definite evidence of infarction on taking further leads. There is nothing new in this observation, of course, but it does emphasize the need for caution.

We are satisfied that further information of material value may be obtained in patients of the type under consideration. The criteria of abnormality vary only in degree from the changes seen in normal controls. It is difficult to draw a definite line between them. Consequently, there is a theoretical danger of false positive tests, that is, of attributing borderline cardiographic changes in healthy hearts to organic disease. Nevertheless, we have no reason to believe that we have ever been misled into diagnosing coronary disease when none was present. It is generally agreed that the present criteria of abnormality make such a mistake most unlikely. In borderline cases the test should be ignored.

An examination of our records reveals that the greatest abnormality is usually shown in a chest lead recorded over the left ventricle. In 9 out of 11 consecutive cases, the degree of S–T depression in lead IV is greater than that in any one of the three standard limb leads and indeed as great as, or greater than, in these three leads added together. Although further experience will be required to establish the point, it is suggested that S–T depression of 2 mm. or more in lead IV indicates a positive test. We have recently been recording multiple chest leads and it seems probable that for routine purposes, Lead IV will prove to be the most suitable lead in that the degree of S–T depression is usually as much as, or more than, in any other lead. Furthermore, in the last eight cases recorded, the changes in unipolar (V) leads and bipolar (CR) chest leads have been compared. In seven of them, the degree of S–T depression in CR leads has been significantly greater than in V leads. This too suggests a possible improvement and simplification in establishing criteria of abnormality.

These points are illustrated in Fig. 6. The limb leads are not in fact quite normal in that there is slight slurring of the QRS complex in Lead II. However, this is not diagnostic of coronary disease. It will be seen that the test is a positive one and the degree of S–T depression is greater in Lead IV than in the three limb leads added together and greater in CR4 than in V4.

Theoretical Aspects

Changes in the S–T segment and T waves similar to those occurring in the anoxæmic test though less marked, may be produced in healthy people by a variety of factors including emotion. In

spite of this, assistance of real value may be given in clinical problems concerning coronary insufficiency. Obviously it is important to consider the relevant factors that may be operative during the test and also the theoretical background for the electrocardiographic changes observed.

Although the ultimate causes of the potential variations responsible for the changes remain largely a mystery the possible factors that initiate them are of practical importance. Our present problem is to distinguish the physiological variants which may occur during the test in normal people from pathological effects which may be seen in subjects with coronary artery disease. For this reason reference must be made to some of these factors which include anoxæmia, ischæmia, emotion, tachycardia, hyperventilation, alkalosis, posture and autonomic imbalance. They are often inter-related.

Other factors which can produce changes in the electrocardiogram should be remembered, e.g. a recent meal (Gardberg and Olsen, 1933; Simonson *et al.*, 1946), an ice-cold drink (Wilson and Finch, 1923), tobacco (Graybiel *et al.*, 1938; Bryant and Wood, 1947), need not be discussed here since they are normally excluded from playing any part during the test.

The changes produced by anoxæmia can be reversed by giving oxygen. The normal heart is remarkably tolerant to anoxæmia partly because of the marked increase in coronary blood flow which occurs though naturally this is limited in subjects with narrowed vessels. The cardiac output is also increased so that if the work of the heart is augmented there may yet be a relative myocardial ischæmia as in the exercise test (Wiggers, 1941). The changes produced by ischæmia are firmly established and similar in type to those under consideration.

Tachycardia, hyperventilation and autonomic imbalance with predominant sympathetic stimulation may all be responsible for the electrocardiographic changes produced by emotion. The effects of tachycardia are usually inseparable from the sympathetic overactivity and lowering or even inversion of the T waves is known to accompany considerable tachycardia from any cause (White *et al.*, 1941). However, tachycardia of sufficient degree does not occur in the anoxæmic test.

Hyperventilation may be responsible for some of the clinical manifestations in anxiety states (Kerr *et al.*, 1937, 1939). Weakness, dizziness, faintness, parathesiae, tachycardia, tremulousness and cramps can be produced by voluntary over-breathing and Thompson (1943) also states that pain simulating angina pectoris may be reproduced in healthy persons and that symptoms may be accompanied by T wave inversion and slight S–T segment depression in the electrocardiogram. Alkalosis is probably the principal but not the sole factor concerned in such cases. Similar changes have been recorded when alkalosis results from other causes (Lawrence and Allott, 1943; Barker *et al.*, 1939). Some degree of hyperventilation is commonly observed during the anoxæmic test but is usually slight and not sufficient to affect the electrocardiogram. It is in fact more likely to occur during the exercise test.

The effects of posture in lowering or inverting the T wave are now well known though there have been varying opinions about the mechanism involved (Leimdörfer, 1935; Åkesson, 1936; Graybiel and White, 1935; White *et al.*, 1941; Scherf and Weisberg, 1941; Master, 1944; Wendkos, 1944; Wendkos and Logue, 1946). This factor was avoided in our cases by taking all records with the subject recumbent.

Autonomic imbalance is presumably responsible for similar changes (of lesser degree) which have sometimes been observed in cases of effort syndrome. Sympathetic stimulation which can be neutralized by giving a sympatholytic drug can produce such changes even in the absence of significant tachycardia (Wendkos and Logue, 1946).

Discussion

It is clear that flattening or inversion of the T waves may occur under such a wide range of circumstances that it is an unreliable sign of coronary insufficiency in the anoxæmic or exercise tests. More attention can be paid to S–T depression although it may also occur in some of the circumstances in which T wave changes are seen. However, from a study of the papers which have been published the significance of S–T depression is largely substantiated and with Levy's method of adding up the total depression in the four leads, a reasonably clear border line between normal and abnormal cases can be drawn. Where the results are near the border line due caution in interpretation is naturally indicated. Usually, however, the test will be either clearly positive or negative. Discussion of the principles of electrocardiographic interpretation involved may be

found in the reviews of Wilson (1944, 1947), Ashman (1940), Eyster and Meek (1942), Bayley (1943, 1946), Katz (1947), Hellerstein and Katz (1948), Pirani and Schlichter (1946) and Price and Janes (1943). In experimental animals (Bayley *et al.*, 1944) temporary myocardial ischæmia has been shown to produce changes in the S–T segment and T waves similar to those observed in the anoxæmic test.

In cardiac infarction S–T displacement is usually upwards but it is commonly downwards both in spontaneous angina and in the anoxæmic test. For these differences good reasons may be advanced. It is known that injury to the sub-epicardial layers will result in upward displacement of the S–T segment as recorded by an overlying electrode and injury to the sub-endocardial in downward displacement. This has been demonstrated in animals and also observed in human myocardial infarction. Also an injury to the sub-epicardial region will result in greater and more persistent electrocardiographic changes than a similar injury to the sub-endocardial region (Hellerstein and Katz, 1948). In the experimental work as in naturally occurring myocardial infarction a layer of sub-endocardial muscle commonly survives and accounts for the fact that the S–T displacement is upwards. The reason for this frequent immunity of the sub-endocardial lamina presumably lies in relatively better nutrition which derives from the collateral blood supply of the sub-endocardial arteriolar plexus of Gross, from the Thebesian vessels and possibly from direct diffusion of oxygen through the endocardial wall from the ventricular cavity. In spontaneous attacks of angina the S–T displacement which is usually seen may be explained by spasm of the sub-endocardial plexus (Bayley, 1946). In the anoxæmic test not only is the blood in the coronary vessels and ventricular cavities inevitably reduced in oxygen content so that there will be little benefit to the sub-endocardial layers but it may be that the latter are abnormally sensitive to oxygen lack since they are accustomed to a superior blood supply (Biörck, 1948).

The theoretical basis for the anoxæmic test is nevertheless not fully established. S–T depression may be caused by physiological changes concerning repolarization or by pathological changes leading to the production of a current of injury. Fortunately, electrocardiograms can usually be interpreted without regard to theory and failure to agree upon, or even understand, the underlying mechanisms has not prevented progress in this field.

Summary and Conclusions

Various procedures which have been recommended for the assessment of coronary insufficiency are briefly reviewed and the history of the anoxæmic test is referred to in some detail. The technique of the anoxæmic test is described and criteria of abnormality and possible reactions discussed. It is suggested that the duration of anoxæmia can be limited to ten minutes. The results of 22 control tests and a study of 33 patients are presented. Assistance of material value may be obtained in difficult cases particularly with regard to atypical pain in the chest. When properly conducted on suitable patients the test is not dangerous.

It is suggested that S–T depression of 2 mm. or more in Lead IV indicates a positive test and that further experience may show that it is unnecessary to record other leads.

It is concluded that the anoxæmic test has a small but useful role to play in the assessment of coronary insufficiency and holds certain advantages over the exercise test.

We should like to acknowledge the considerable help received from members of the Anæsthetic Staff of the Western General Hospital, and also to the physicians who have referred their cases.

References

Åkesson, S. (1936). *Upsala Läkaref Forh*, **42**, 263. (Quoted by White, P. E., *et al.* (1941). *Brit. Heart J.*, **3**, 233).
Ashman, R., Wilde, W. S., and Drawec, E. (1940). *Amer. J. Physiol.*, **128**, 547.
Barker, P. S., Schrader, E. L., and Ronzoni, E. (1939). *Amer. Heart J.*, **17**, 169.
Bayley, R. H. (1943). *Amer. Heart J.*, **26**, 769.
—— (1946). *Amer. Heart J.*, **31**, 677.
——, La Due, J. S., and Yorke, D. J. (1944). *Amer. Heart J.*, **27**, 164 and 657.

Biörck, G. (1946*a*). *Amer. Heart J.*, **32,** 689.
—— (1946*b*). *Brit. Heart J.*, **8,** 17.
——, Jackson, F. S., and Rohlin, A. (1948). *Acta. Med. Scand.*, **82,** 283.
Bryant, J. M., and Wood, J. E. (1947). *Amer. Heart J.*, **34,** 20.
Burchell, H. B., Pruitt, R. D., and Barnes, A. R. (1948). *Amer. Heart J.*, **36,** 373.
Burnett, C. T., Nimms, M. G., and Josephson, C. J. (1942). *Amer. Heart J.*, **23,** 306.
Cottrel, J. E., and Wood, F. C. (1931). *Amer. J. med. Sci.*, **181,** 36.
Dripps, R. D., and Comroe, J. H. (1947). *Amer. J. Physiol.*, **149,** 277.
Evans, C., and Bourne, G. (1940). *Brit. Heart J.*, **3,** 69.
Eyster, J. A. E., and Meek, W. J. (1942). *Amer. J. Physiol.*, **138,** 166.
Gardberg, M., and Olsen, F. (1933). *Amer. Heart J.*, **17,** 725.
Graybiel, A., and White, P. D. (1935). *Amer. Heart J.*, **10,** 345.
——, Starr, R. S., and White, P. D. (1938). *Amer. Heart J.*, **15,** 89.
Greene, C. W., and Gilbert, N. C. (1921). *Arch. intern. Med.*, **27,** 517.
Grossman, M., Weinstein, W. W., and Katz, L. N. (1949). *Ann. intern. Med.*, **30,** 387.
Hellerstein, H. K., and Katz, L. N. (1948). *Amer. Heart J.*, **36,** 184.
Katz, L. N. (1947). *Physiol. Rev.*, **27,** 398.
——, Hamburger, W. W., and Lev, H. (1932). *Amer. Heart J.*, **7,** 371.
——, ——, and Schutz, W. J. (1934). *Amer. Heart J.*, **9,** 771.
Kerr, W. J., Dalton, J. W. and Gliebe, P. A. (1937). *Ann. intern. Med.*, **11,** 961.
——, ——, Soley, M. H., and Shock, N. W. (1939). *J. Amer. med. Ass.*, **113,** 637.
Kountz, W. B., and Gruber, C. M. (1929). *Proc. Soc. Exper. Biol. Med.*, **27,** 171.
Larsen, K. H. (1938). *Copenhagen, Ejnar Mundsgaards Forlag.* (Quoted by Levy, 1941*a*).
Lawrence, J. S., and Allott, E. M. (1943). *Brit. Heart J.*, **5,** 128.
Leimdörfer, A. (1935). *Med. Klin.*, **31,** 1536. (Quoted by White, P. D., *et al.* (1941). *Brit. Heart J.*, **3,** 233).
Levine, S. A., Ernstene, A. C., and Jacobson, B. M. (1930). *Arch intern. Med.*, **45,** 191.
Levy, R. L. (1946). *Modern Concepts of Cardiovascular Disease*, **15,** No. 4.
——, Barach, A. L., and Bruen, H. G. (1938). *Amer. Heart J.*, **15,** 187.
——, Bruen, H. G., and Russell, N. G. (1939). *Amer. J. med. Sci.*, **197,** 241.
——, Patterson, J. E., Clark, T. W., and Bruen, H. G. (1941*b*). *J. Amer. med. Ass.*, **117,** 2113.
——, Williams, N. E., Bruen, H. G., and Carr, H. A. (1941*a*). *Amer. Heart J.*, **21,** 634.
Malmström, A. (1947). *Acta Physiol. Scand.*, **125,** suppl. 195.
Mannheimer, E. (1946). *J. Pediatrics.*, **29,** 1.
——, and Carlgren, L. E. (1948). *J. Pediatrics.*, **33,** 1.
Master, A. M., Friedman, R., and Dack, S. (1942). *Amer. Heart J.*, **24,** 777.
——, Nuzie, S., Brown, R. C., and Parker, R. C. (1944). *Amer. J. med. Sci.*, **207,** 435.
Nylin, G. (1943). *Nordisk. Med.*, **18,** 1045. (Quoted by Biörck, 1946).
——, and Grewin, K. E. (1942). *Cardiologia*, **6,** 169. (Quoted by Biörck, 1946).
Patterson, J. E., Clark, T. W., and Levy, R. L. (1942). *Amer. Heart J.*, **23,** 837.
Penneys, R., and Thomas, C. B. (1948). *Bull. Johns Hopkins Hosp.*, **82,** 470.
Pirani, C. L., and Schlichter, J. G., (1946). *Ann. intern. Med.*, **25,** 847.
Price, R. K., and Janes, L. R. (1943). *Brit. Heart J.*, **5,** 134.
Resnik, W. H. (1925). *J. Clin. Invest.*, **2,** pp. 93, 117 and 125.
Riseman, J. E. F., Waller, J. V., and Brown, M. G. (1940). *Amer. Heart J.*, **19,** 683.
Rothschild, M. A., and Kissin, M. (1933). *Amer. Heart J.*, **8,** pp. 729 and 745.
Ruskin, A. (1947). *Amer. Heart J.*, **34,** 569.
Scherf, D., and Weisberg, J. (1941). *Amer. J. med. Sci.*, **201,** 693.
Simonson, E., Alexander, H., Henschel, A., and Keys, A. (1946). *Amer. Heart J.*, **32,** 202.
Stewart, H. J., Horger, E. L., and Sorenson, C. W. (1948). *Amer. Heart J.*, **36,** 161.
Thompson, W. P. (1943). *Amer. Heart J.*, **25,** 372.
Ward, G. E. S., and Wright, S. (1929). *Lancet*, **2,** 1184.
Weintraub, H. J., and Bishop, L. F. (1947). *Ann. intern. Med.*, **26,** 741.
Wendkos, M. H. (1944). *Amer. Heart J.*, **28,** 549.
———, and Logue (1946). *Amer. Heart J.*, **31,** 711.
White, P. D., Chamberlain, E. L., and Graybiel, A. (1941). *Brit. Heart J.*, **3,** 233.
Wiggers, C. (1941). *Ann. intern. Med.*, **14,** 1237.
Wilson, F. N., and Finch, R. (1923). *Heart*, **10,** 275.
——, Johnston, F. D., Rosenbaum, F. F., Erlanger, M., Kossman, C. E., Hecht, H., Kotrim, N., de Oliveira, R., and Barker, D. S. (1944). *Amer. Heart J.*, **27,** 19.
——, Rosenbaum, F. F., and Johnston, F. D. (1947). *Advances in Internal Medicine*, **2,** 52.

CASE REPORTS

A CASE OF VENTRICULAR FIBRILLATION

BY

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A case of complete heart block with paroxysms of ventricular fibrillation, during the last night of her life is reported.

Case Report

A woman, aged 85, was admitted to Harrogate General Hospital under the care of Mr. Gordon Bailey on May 30, 1950 with vomiting and constipation that had been present for four days. Heart block had been diagnosed by her family doctor three weeks before.

Her pulse was irregular, 32 a minute; the blood pressure was 230/90. She vomited repeatedly and gastric suction and intravenous saline were started to combat dehydration.

On June 2 her vomiting had ceased; she was seen by Dr. Curtis Bain and a diagnosis of complete heart block with premature ventricular beats was made. The heart was not enlarged, but persistent crepitations were audible at the base of the left lung.

On June 4 the patient developed attacks of unconsciousness lasting a few seconds, in which she became pulseless and cyanosed, with tonic and clonic movements of the limbs. The attacks became more frequent and she died on June 9.

A cardiogram taken on June 6 showed complete heart block with an auricular rate of 100 and the Q–T time greatly prolonged, 0·72 sec. (Fig. 1). The ventricular rhythm was irregular due to multifocal ectopic beats, the rate being about 36. A short paroxysm of ventricular tachycardia is shown, preceded by an initial premature beat. The latter follows the preceding ventricular complex by an interval of 0·68 sec. and is directed downwards (Fig. 2).

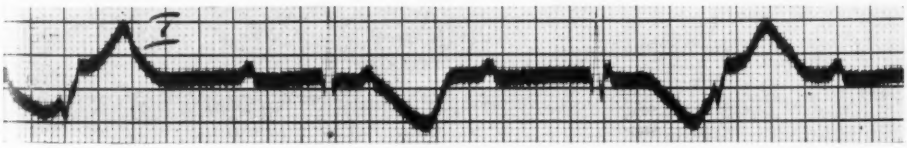

FIG. 1.—Complete heart block. Q–T time 0·72 sec., auricular rate 100.

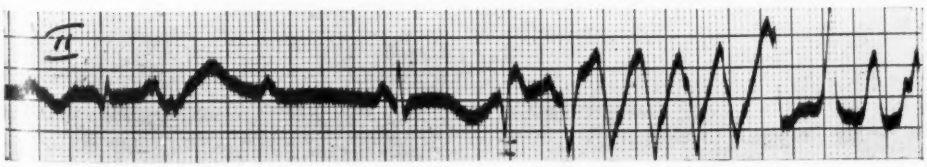

FIG. 2.—Multifocal ectopic beats. Initial premature beat (I) follows preceding beat after 0·68 sec. Ventricular tachycardia.

The final set of cardiograms was taken on the night of June 8 between 8 p.m. and 11 p.m. The patient died at 12.15 a.m. on June 9.

Several short paroxysms of ventricular tachycardia and ventricular fibrillation occurred and the auricular rate increased to 120 a minute (Fig. 3).

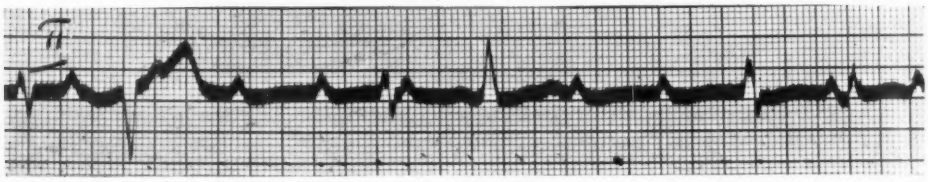

FIG. 3.—Multifocal ectopic ventricular beats. Auricular rate 120.

Short paroxysms of ventricular tachycardia occurred without ensuing fibrillation (Fig. 4); and they usually ended in a short pause during which one or two auricular beats occurred before the idioventricular rhythm was resumed.

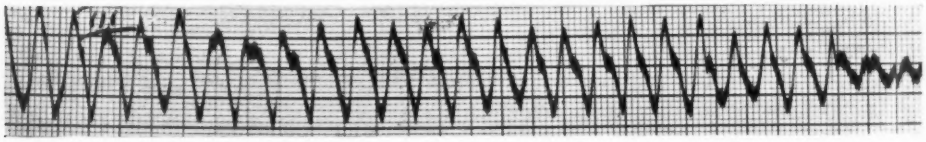

FIG. 4.—Paroxysm of ventricular tachycardia.

Fig. 5 shows the end of a paroxysm of ventricular tachycardia: a short pause is followed by multifocal ectopic ventricular beats, and these are followed by a short period of ventricular fibrillation (Fig. 6).

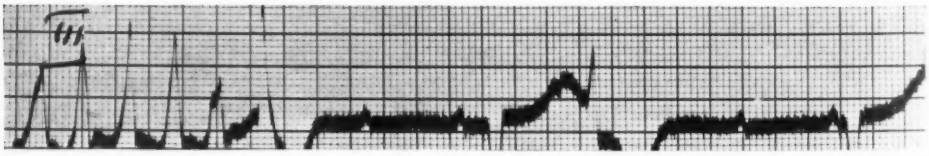

FIG. 5.—End of paroxysm of ventricular tachycardia followed by multifocal ectopic beats.

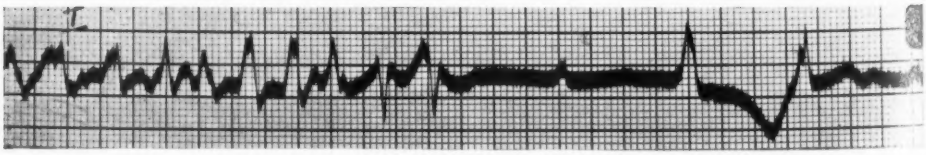

FIG. 6.—Short bout of ventricular fibrillation (initial fibrillary period) ending in ectopic ventricular beats.

Fig. 7 shows the end of a bout of ventricular tachycardia leading into what looks like ventricular flutter at a rate of 300. This is followed by ventricular fibrillation; the waves become irregular in size and duration and the ventricular rate has increased once more (Fig. 8).

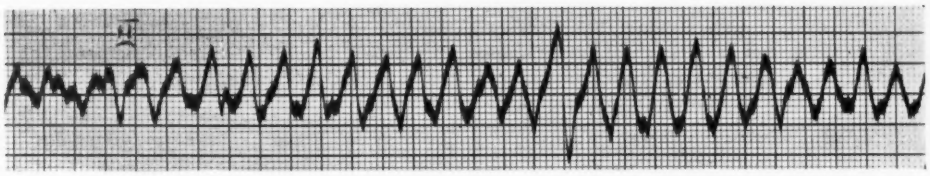

FIG. 7.—Ventricular tachycardia leading into ventricular flutter (Rate 300).

FIG. 8.—Ventricular fibrillation (Rate about 400).

Following the paroxysm of ventricular fibrillation there was an undulatory pause of about five seconds, a solitary ventricular complex occurring at the end of the pause (Fig. 9). During this pause

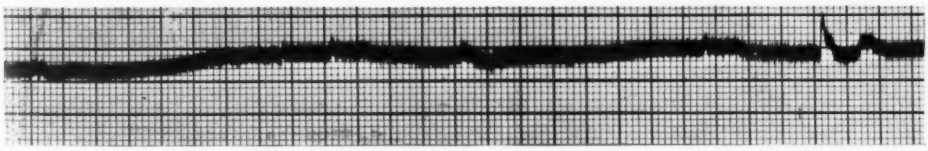

FIG. 9.—Post-undulatory pause of 5 seconds. Auricular rhythm irregular. Solitary ventricular complex at the end of the pause.

the auricles beat irregularly. Finally an idioventricular rhythm is resumed (Fig. 10). Terminal cardiograms of this case were not, unfortunately, obtained.

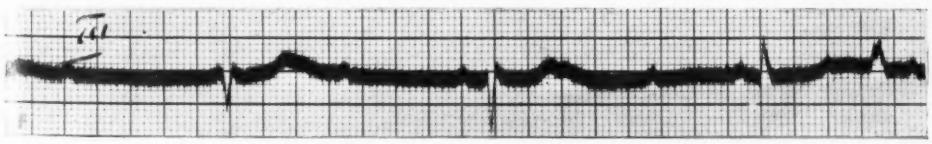

FIG. 10.—Complete heart block resumed after paroxysm of ventricular fibrillation.

Discussion

Ventricular fibrillation is well known as an agonal phenomenon. The fact that it occurs in episodes followed by recovery is not so well recognized.

Robinson and Bredeck published the first case of ventricular fibrillation with recovery in 1917. Schwartz (1942) described as many as three hundred attacks occurring in the same patient in twenty-four hours. His paper illustrates three phases in the development of ventricular fibrillation.

(1) *Prefibrillary stage.* The development of ventricular fibrillation depends on an increase in the basic ventricular rate; and this can occur in several ways, as shown in the electrocardiograms of the present case. Ventricular tachycardia followed by multifocal ectopic beats leads into ventricular fibrillation (Fig. 5 and 6). Schwartz (1942) calls the ectopic beat that initiates the run of tachycardia preceding fibrillation, the initial premature beat (Fig. 2). This bears a constant time relationship to the preceding ventricular complex, and all such initial beats are similar in form and direction. The occurrence of such beats supports the view that an irritable focus in the ventricular muscle is a precursor of ventricular fibrillation. A prolonged attack of ventricular fibrillation is preceded by shorter periods, called initial fibrillary periods (Schwartz, 1942); these are apparently peculiar to the human heart (Fig. 6).

(2) *Fibrillary stage.* The curve is quite characteristic, the complexes are deformed and variable in size resembling an artefact rather than an electrocardiogram. They may, however, be preceded by ventricular oscillations varying in height from 8–10 mm. at a rate of 280 to 300 a minute (Fig. 7). Schwartz calls this ventricular flutter, but other authors do not consider this term justifiable (Parkinson *et al.*, 1941).

(3) *A post-undulatory pause* always follows a bout of fibrillation, the longest recorded being 79 seconds (Parsonnet *et al.*, 1946). When the preceding fibrillary period is long the auricles may stop beating, or beat irregularly during the pause (Fig. 9). Some hours later auricular fibrillation or flutter may appear.

Summary

A case is presented of complete heart block with paroxysms of ventricular fibrillation.

I wish to thank Dr. Curtis Bain and Mr. Gordon Bailey for permission to publish this case.

References

Parkinson, J., Papp, C., and Evans, W. (1941). *Brit. Heart J.*, **3**, 171.
Parsonnet, A. E., Bernstein, A., and Klosk, E. (1946). *Amer. Heart J.*, **31**, 769.
Robinson, G. C., and Bredeck, J. F. (1917). *Arch. intern. Med.*, **20**, 725.
Schwartz, S. P. (1942). *J. Mount Sinai Hospital*, **8**, 1005.

COARCTATION OF THE AORTA

BY

M. McGREGOR AND M. MEDALIE*

From the Cardio-Pulmonary Research Unit (Council for Scientific and Industrial Research) of the Department of Medicine, University of the Witwatersrand and Johannesburg General Hospital

Several anomalies of the great vessels have been described in association with coarctation of the aorta. The case presented below had unusual features which seem worthy of placing on record. In addition, a technique of simultaneous angiocardiography and retrograde aortography is described.

Case Notes

The patient was an eight-year-old white boy who had always been noted to tire rather easily and to complain of abdominal pain after strenuous exertion. Recently symptoms had increased.

On examination he was thin (height, 54 inches; weight, 47 lb.) but was otherwise a normal intelligent child. The most striking feature was the prominence and tortuosity of both carotid vessels which stood out under the skin of the neck. On palpation they were tense and seemed to contain blood at a very high pressure. Elsewhere, there was complete absence of arterial pulsation and the blood pressure could not be ascertained. No scapular or other collateral vessels could be felt.

Cardiac examination showed a heaving apex beat of left ventricular type in the mid-axillary line, and there was slight prominence of the left præcordium. A faint systolic thrill was palpable in the suprasternal notch. On auscultation over the apex, a grade 2 (Levine, 1949) blowing systolic and a grade 4 rumbling mid-diastolic murmur were heard. From the left second to fifth interspaces there was a loud (grade 4) blowing systolic murmur followed by a normally split second sound of average intensity. Over the whole of the skull a fairly loud rumbling continuous murmur typical of arterio-venous aneurysm was present; no point of maximal intensity could be found.

The fundi showed the features of hypertensive retinopathy. The arteries showed irregular zones of contraction and in the right fundus there was some papillœdema with numerous exudates and a macula star. The diastolic blood pressure in the retinal artery was about 200 mm. of mercury. The rest of the physical examination was negative.

The diagnosis of coarctation of the aorta with severe hypertension of the cerebral circuit and much enlargement of the left ventricle could be made on clinical grounds alone. In addition, it seemed probable that both subclavian arteries arose in or below the coarcted segment. The continuous murmur over the head was possibly due to an arteriovenous aneurysm. However, as localization was not possible, it was more likely that the murmur developed in the greatly dilated channels caused by the increased flow in the carotid vessels. In addition, mitral stenosis was suspected.

Investigations. Apart from a mild anæmia (red cells, 3·8 million per cu. mm.) the blood count was normal. The sedimentation rate was 3 mm. in one hour and the Wassermann reaction was negative.

Phonocardiograms confirmed the presence of the murmurs that had been heard, and electrocardiograms showed the pattern of left ventricular strain.

Routine X-ray examinations did not add to the diagnosis but confirmed several points. In the postero-anterior view the aortic knuckle appeared normal and there was no rib notching. There was much cardiac enlargement affecting chiefly the left ventricle. The pulmonary vessels appeared

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normal and the lungs seemed normally vascularized. There was evidence of left atrial enlargement, both in the postero-anterior and in the right anterior oblique views. In the latter view an indentation of the posterior wall of the barium filled œsophagus confirmed the presence of an anomalous right subclavian artery, while in the left anterior oblique view considerable enlargement of the left ventricle was observed.

In an attempt to learn as much as possible of the vascular anomalies in this case before resorting to surgery, a routine antero-postero angiocardiogram was performed employing the now widely used technique of Robb and Steinberg (1939) with a cassette changer and certain modifications to the syringe previously described (McGregor, 1949 and 1951). As will be seen (Fig. 1A), two dilated and tortuous carotid vessels were seen to be arising from an otherwise normal aortic arch which ended suddenly at the commencement of the descending aorta. No diodrast entered the distal segment and no collateral vessels could be seen.

In view of the failure of the distal segment to fill with diodrast it was impossible to learn the length of the stenosed segment. Accordingly, two days later the patient was anæsthetized and while a cannula was inserted into an arm vein in the usual manner the femoral artery was exposed, and under screen control a large (No. 10) catheter was passed up the abdominal aorta. The patient was placed in the right posterior oblique position and 25 ml. 70 per cent diodrast followed by 15 ml. saline was injected into the arm vein. After four seconds, injection of 15 ml. diodrast was started via the catheter inserted into the femoral artery. Exposures were taken throughout at the rate of approximately three per second. The resultant plates showed a normal right heart and pulmonary artery (Fig. 1B). During filling of the systemic circuit (Fig. 1C) a better view of the aortic arch and origin of the carotids was obtained. There was adequate filling of the descending aorta which appeared normal and it could be seen that the coarcted segment was extremely short, rendering an aortic graft unnecessary. The subclavian arteries did not appear to fill from either the upper or lower segments.

A B C

FIG. 1.—Angiocardiograms from this case. (A) After routine angiocardiogram, showing two dilated and tortuous carotid arteries and the absence of filling of the descending aorta. (B) Normal right side of the heart after routine angiocardiography in the right posterior oblique position, also showing a catheter that has been inserted through the femoral artery. (C) The same, but later, showing the left side of the heart: the second injection has been given through the catheter to show the descending aorta (see text).

Progress. Following the first visit the patient's condition deteriorated rapidly. He developed a partial left facial paralysis, complete loss of vision in the left eye, and early left ventricular failure within the next seven weeks. After digitalization had produced some improvement in condition, surgery was attempted, but the patient died in cardiac arrest during the opening of the thorax.

Post-mortem Summary. Post mortem, an unusually high coarctation of the aorta was found below the insertion of a just patent ductus arteriosus (Fig. 2, F). The aortic arch (A) was dilated but the descending aorta (E) and pulmonary vessels (G) were normal. Both subclavian arteries (B and D) arose distal to the coarctation, the right subclavian being aberrant in course. No dilated intrathoracic collaterals were seen. The carotid vessels (C) showed atherosclerotic changes and there was gross dilatation and atherosclerosis of all the intracerebral vessels. The heart showed dilatation and hypertrophy of the left ventricle, and small vegetations were found along the free edge of the mitral valve though the mitral valve was not actually stenosed. The aortic valve was bicuspid.

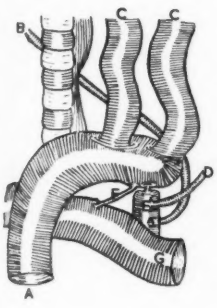


FIG. 2.—Diagrammatic representation of the abnormal arteries showing both subclavians arising below the coarctation. (A) Aorta. (CC) Carotid arteries. (B) Right and (D) left subclavian arteries. (E) Descending thoracic aorta. (F) Slightly patent ductus arteriosus. (G) Pulmonary arteries.

Comment

An anomalous right subclavian artery in association with coarctation of the aorta is extremely rare. In a case reported by Fawcett (1905), and in a post-mortem specimen described by East (1932) the anomalous right subclavian arose proximal to the point of coarctation. In a third case described by Stevens, there was an anomalous left subclavian arising below the coarctation (Gross, 1950.)

The clinical features in our case were striking and were such that the anomaly could be diagnosed with reasonable certainty on clinical grounds alone. It has now become important to define with accuracy the exact length of the coarcted segment. In most cases the length of this can be ascertained from routine angiocardiograms or aortograms via the radial artery, but as in this case, simultaneous angiocardiography and retrograde aortography via the abdominal aorta may sometimes be needed.

Summary

An unusual case of coarctation of the aorta is described in which both subclavian vessels arose below the site of narrowing. Anomalies of the carotid vessels were also present. Pulses in all four limbs were absent and there was none of the usual evidence of the collateral blood supply to the lower extremities. In order to demonstrate the length of the constricted segment, simultaneous angiocardiography and retrograde aortography was employed.

Our thanks are due to Professor G. A. Elliott and Dr. T. H. Bothwell for helpful criticism in writing this paper. We also wish to acknowledge with gratitude the assistance of our colleagues Dr. J. L. Braudo and Dr. J. Lannon; also Dr. J. Kaye of the Department of Radiology of the Johannesburg Hospital and the members of his staff, and lastly to Dr. R. E. Gross of the Peter Bent Brigham Hospital, Boston, Massachusetts, for his kind assistance and for permission to print the post-mortem findings.

REFERENCES

East, T. (1932). *Proc. Roy. Soc. Med.*, **25**, 797.
Fawcett, J. (1905). *Guy's Hosp. Reports*, **59**, 17.
Gross, R. E. (1950). *Circulation*, **1**, 41.
Levine, S. A., and Harvey, W. P. (1949). *Clinical Auscultation of the Heart.* W. B. Saunders and Company, London.
McGregor, M. (1949). *Brit. J. Radiol.*, **22**, 459.
——, (1951). *Brit. J. Radiol.*, **24**, 226.
Robb, G. P., and Steinberg, I. (1939). *Amer. J. Roentgenol.*, **41**, 1.

COAL-GAS POISONING AND CARDIAC SEQUELÆ

BY

MONTAGUE HADLEY

From the Royal Infirmary, Edinburgh

The comparative infrequency of coal-gas poisoning may lead those who are not familiar with the subject to deal perfunctorily with victims, and to regard active treatment as unnecessary.

The majority of coal-gas poisoning victims in the South-Eastern region of Scotland are admitted to Edinburgh Royal Infirmary, treatment having been started en route. From a study of 272 such cases occurring during the last decade, only 0·7 per cent were found to show major cardiac sequelæ. The following case is presented, therefore, as a rarity, and substantiates the foregoing tenets.

Case Notes

Mr. F. S., aged 53 years, led a strenuous outdoor life on a small island, and had never been ill in his life, until he was overcome by petrol exhaust gas whilst attending to his motor-boat engine. After an interval of about one hour, he was discovered and removed to bed, but received no treatment. Gradually, after 36 hours, he regained consciousness, and thereafter his recovery was slow, retarded by vomiting and severe nausea. He noted that his chest and left arm were peppered with petechiæ, which rapidly disappeared. Five days after this episode, he felt no obvious ill-effects, and returned to his work, but while attempting to find the leak in the exhaust-pipe that caused the previous mishap, he was again rendered unconscious. He was discovered 20 minutes later, and regained consciousness in three hours. He experienced no untoward effects, apart from nausea, vomiting, and loss of appetite, and he was able to carry on with heavy manual work on the following day.

Fourteen days after the primary gassing, while working, he developed angina of effort, with radiation of the pain into his neck and down to his left wrist. Symptoms recurred on exertion, and were accompanied by a gripping sensation in his throat. He slept well and did not complain of breathlessness or swelling of the ankles.

These anginal attacks increased in frequency and severity so rapidly that seven days later, when coming for a medical examination, his tolerance was reduced to two hundred yards on the flat. Rest still relieved the pain, but he was now developing a concomitant breathlessness.

The family history was free from disease, and gave no specific evidence of heart disease or premature deaths.

On examination, he was a ruddy-complexioned, alert man of 53 years, with no evidence of cyanosis, venous congestion, or peripheral œdema. Examination of the chest revealed no abnormality, the heart being of normal size, in normal rhythm, and without murmurs. The blood pressure was 135/85. Crepitations were present at the left lung base. No abnormality was elicited in any other system.

Examination of the urine showed it to be free from albumen and sugar. The Wassermann reaction was negative. The hæmoglobin was 97 per cent and the red blood corpuscle count 4·7 million. The B.S.R. was 8 mm./hr. (Westergren). X-ray revealed nothing more than a little prominence of the aortic arch. The lung fields were normal. The electrocardiogram showed sinus bradycardia at 56 a minute, a P–R interval of 0·16 sec., no axis deviation, and T waves inverted in lead I, and upright in leads II and III. In the unipolar leads, aVR and aVL were similar, with inverted P and T waves, and Q as the sole initial deflection. In aVF there was a tiny Q, tall R and an upright T wave.

V1 to V3 were similar with small R, deep S, and upright T waves. The transitional zone was between V4 and V5. In V5 there was a tall R, small S, marked S–T depression and sharply diphasic T wave. In V6, R was the sole initial deflection, measuring 30 mm. There was slight S–T depression and inverted T wave.

It was evident that he was suffering from myocardial ischæmia. We are justified in considering the two anoxial episodes as the precipitating factors, as effort pain commenced in a previously fit man so soon after such a severe constitutional upset.

He was sent home and advised to have complete rest in bed. Twenty-four hours later, while in bed, he developed severe præcordial pain and suddenly died. No autopsy was performed, and death was presumed to be due to coronary thrombosis.

Commentary

The major constituent of exhaust gas is carbon monoxide, which has the property of uniting with hæmoglobin when it comes into contact with blood to form carboxyhæmoglobin, exactly replacing the oxygen volume for volume and thus rendering the blood unavailable for oxygen carriage. Apart from carbon monoxide, exhaust gas also contains a varying percentage of hydrocarbons, of which benzol is a known tissue poison, and it was noted by Winslow (1927) that when it was present in petrol exhaust fumes, the toxicity of the gas, in comparison with coal gas, was increased. The important factor in the above case, however, is anoxia, for gassing was rapid and in a confined space. The effect of the necrotoxins is negligible, under these circumstances, compared with the effects of asphyxia.

Haggard (1921) observed that acute oxygen deficiency produced a function impairment of A-V conduction and Steinmann (1937) confirmed this, giving the frequency of electrocardiographic changes found in patients suffering from coal-gas poisoning as an example. In anoxia, it is generally observed that the most specialized tissue suffers first and, therefore, any damage to the heart would affect the A-V node, S-A node, and bundle of His. Experimental asphyxias produced in cats by Lewis *et. al.* (1914) confirmed this premise, and the results in these animal experiments were found applicable to man by Greene and Gilbert (1921), who were of the opinion that any disturbance below the branching of the bundle of His was permanent. Colvin (1928), however, describes a case of coal-gas poisoning where cardiographic changes suggested damage below the bundle of His in a healthy young man; this apparent damage rapidly and completely disappeared. In the pre-critical stage of gassing, there is shortening of the P–R interval, and in the post-critical stage a tendency for the A-V node to supplant the S-A node as pacemaker, and slowing of the heart rate follows. In the case reported, there was no evidence of impairment of the conduction mechanism, but the cardiograph shows changes in V5 in the form of the S–T segments that one would interpret as being due to a myocardial ischæmia, the form of V6 suggesting left ventricular hypertrophy.

Pathological changes in the heart following coal-gas poisoning were first described by Klebs in 1865, when he reported punctiform and diffuse hæmorrhages into the pericardium, including the tips of the papillary muscles. Gurich (1926) reported similar post-mortem findings in four previously healthy people who had died from coal-gas poisoning: there were hæmorrhagic necrotic foci, with surrounding leucocytic infiltrations, most marked in the septum and papillary muscles of the left ventricle. Similar changes have been noted by Fishberg (1940). Unfortunately, no necropsy was carried out in this case.

Treatment

There is no specific treatment for these patients who show impairment of cardiac function following a gassing episode, but in all cases of gassing, immediate treatment is important.

Rescue workers in mines, abmulance drivers, etc., are taught to remove the victim from the noxious atmosphere, to keep them absolutely at rest, and to combat shock in order that the metabolism and oxygen consumption be reduced to a minimum. A mixture of 93 per cent oxygen and 7 per cent carbon dioxide should be inhaled; if this is not available, artificial respiration is an alternative; carbon monoxide will be eliminated as quickly as possible, and in the victims suspected of having sustained cardiac damage, such treatment is imperative to permit normal conductivity, restricting irreversible processes to a minimum.

Tables compiled from patients admitted to the Royal Infirmary, Edinburgh, suffering from coal-gas poisoning, show that unconsciousness does not occur until the blood level of carbon monoxide

reaches 40 per cent or over, death occurring at a level of 55 per cent or over. In the case reported, the patient's carboxyhæmoglobin lay between 40 and 50 per cent. It is known that the rate of elimination of carbon monoxide from the blood in a given period after exposure varies directly with the initial saturation and it appears the same for the same range of saturation. Thus, in the case quoted, with a carboxyhæmoglobin figure of 40 to 50 per cent, saturation, it would have taken at least ten hours for the carbon monoxide to have been eliminated completely following recovery of consciousness (Sayers and Yant, 1923). Had active treatment been available, this period of partial anoxia (in all, 48 hours) would have been reduced to two hours.

Summary

A case of petrol-exhaust gas poisoning is reported, the victim dying from coronary thrombosis.

My thanks are due to Dr. J. K. Slater and to Dr. Henry Matthew, for their co-operation in allowing me access to their cases and clinical material, and for their advice.

References

Colvin, L. T. (1928). *Amer. Heart J.*, **3**, 484.
Fishberg, A. M. (1940). *Heart Failure*. 2nd ed., 325.
Greene, C. W., and Gilbert, N. D. (1921). *Arch. intern. Med.*, **27**, 517.
Gurich, — (1926). *Abstr. J. Amer. med. Ass.*, **86**, 455.
Haggard, H. W. (1921). *Amer. J. Physiol.*, **56**, 390.
Klebs, E. (1865). *Virchow. Archiv. path. anat.*, **32**, 450.
Lewis, T., White, P. D., and Meakins, J. (1914). *Heart*, **5**, 289.
Steinmann, B. (1937). *Ztschr. Kreislauff*, **29**, 281.
Sayers, R. R., and Yant, W. R. (1923). *Pub. Health Rep. U.S.*, **38**, 2053.
Winslow, C. E. A. (1927). *J. Indust. Hyg.*, **9**, 61.

RUPTURE OF THE INTERVENTRICULAR SEPTUM

BY

BYRON EVANS AND W. F. ANDERSON

From the United Cardiff Hospitals

In 1845 Latham recorded the first case of rupture of the interventricular septum following a cardiac infarction. Sager (1934) found only one case in which a diagnosis had been established ante mortem. Fowler and Failey (1948) found fifty-eight reported cases and in seventeen of these a clinical diagnosis had been made; this number has now increased to twenty-three. During 1950 three cases of septal perforation were seen by us and in all the diagnosis was made before death.

Case Reports

Case 1. A man, aged 61, had been in good health until November, 1949, when he had angina of myocardial ischæmia. Three days later he developed typical symptoms of cardiac infaction. There was no clinical evidence of cardiac enlargement and there were no murmurs. Three weeks later he awoke in the early hours of the morning with severe, sharp and shooting pain in the left breast which continued for two hours. He was short of breath and sweated profusely. On the next day, the apex beat was displaced outwards and a systolic thrill was present in the fourth intercostal space to the left of the sternum. In this area there was a loud, harsh systolic murmur. The diagnosis of perforation of the interventricular septum following cardiac infarction was made.

The cardiogram (Fig. 1) showed inversion of the T wave in lead I with S–T elevation here and in all chest leads (V1 to V7), where deep Q waves were also present. The radiograms (Fig. 2) showed enlargement of the left and right ventricles and hilar congestion.

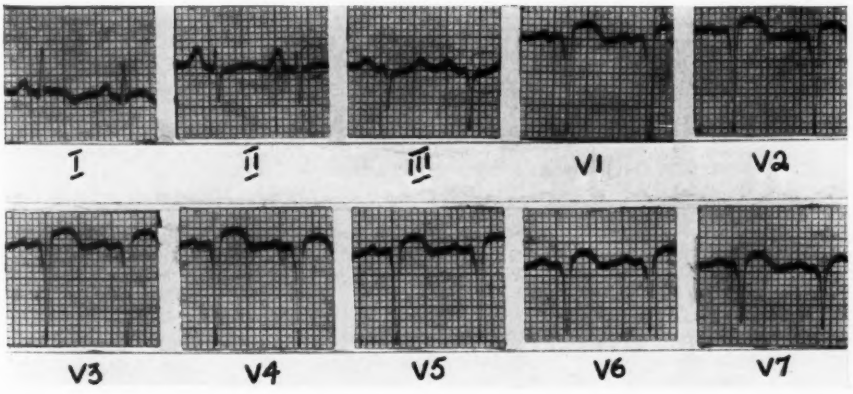
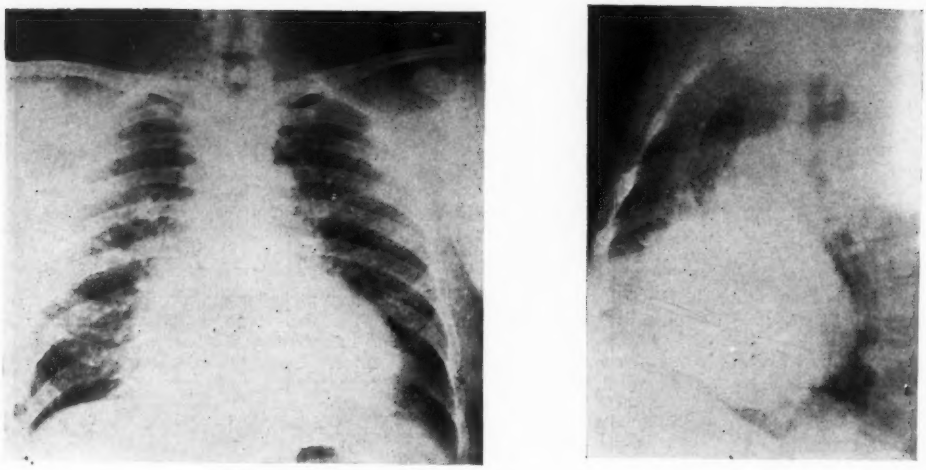


FIG. 1—Case 1 (27/1/50). S–T elevation and inverted T in I; deep Q and S–T elevation in all chest leads.

In October, 1950, he had an attack of severe retrosternal pain of two hours duration, which radiated into the back, the neck and to the shoulders. His condition deteriorated rapidly and he was admitted to hospital. There were obvious signs of heart failure. The pulse was regular and small, the rate was 120 a minute, and the blood pressure could not be recorded. The apex beat was in the anterior axillary line and the systolic thrill was now felt in the mid-clavicular line. The maximum intensity of the loud systolic murmur was one inch external to the midclavicular line in the fifth space.



A B

FIG. 2—Case 1 (27/1/50). (A) Postero-anterior view. (B) Left oblique view. Enlargement of left and right ventricles. Hilar congestion.

The cardiogram was hardly altered from the first tracing; the deep Q waves, especially in the left ventricular chest leads, remained as the most significant finding; there was no added evidence of right heart preponderance. A radiogram with portable apparatus showed more enlargement of the heart and much pulmonary congestion. The patient died the day after admission, one year after the onset of cardiac pain and approximately eleven months after the rupture of the interventricular septum.

Necropsy (Dr. D. B. Richards). The heart weighed 520 g. Both ventricles were hypertrophied (right, 0·9–1·0 cm. thick; left, 1·7–1·9 cm.). The left ventricle showed a healed infarct involving the lower halves of the anterior wall and septum. The ventricular wall in the infarcted area was thin and fibrotic (2–3 mm. thick) and covered by laminated thrombus. At the posterior part of the septum, at the edge of the infarct, was an interventricular communication, crescentic in shape and measuring 0·5 cm. along vertical axis and 0·25 cm. wide. The endocardium around the defect on the right side of the septum was thickened and opaque. The left coronary artery showed marked atheroma with foci of calcification and soft pultaceous areas; the vessel was occluded 2·5 cm. from the origin of the left descending branch for a distance of 3 cm. by organized thrombus. The right coronary artery showed severe atheroma and was occluded 2·5 cm. from its origin by recent red thrombus, which extended for 3·5 cm.

Case 2. A man, aged 57, was admitted to the hospital on September 1, 1950. His health had been good until 16 days before, when he had severe and persistent retrosternal pain. When seen two hours later he was grey in colour and the skin was cold and moist. The heart sounds were distant and there were no murmurs. He made good progress until four days before admission when he suddenly awoke with epigastric pain radiating to the upper chest. When seen in hospital the pulse was barely perceptible and the blood pressure could not be recorded. The heart rate was 120 a minute. The apex beat was displaced one inch beyond the midclavicular line. There was no thrill. A loud blowing systolic murmur was heard all over the præcordium with its maximum intensity in the fourth interspace at the left sternal border. Signs of heart failure were present. A clinical diagnosis of rupture of the interventricular septum following a cardiac infarction was made.

The cardiograms initially showed auricular tachycardia with 3 to 1 (as a rule) A-V block, and later sinus rhythm, with inverted T waves in lead II and III. Radiograms with portable apparatus showed enlargement of right and left ventricles, pulmonary congestion, and bilateral pleural effusions.

Signs of heart failure increased and he died on October 29, 63 days after the rupture of the septum.

Necropsy (Dr. D. B. Richards). The heart weighed 420 g. and was enlarged from dilatation of right ventricle (muscle, 0·4–0·5 cm. thick) and hypertrophy of the left (muscle, 1·6–1·7 cm. thick). There was a large globular thrombus in the right auricular appendage and an oval thrombus 2 × 1·5 × 1·5 cm. adherent to the margin of the coronary sinus. A healed infarct involved the upper two-thirds of the posterior part of the septum and posterior wall of the left ventricle; its upper border extended to within 1·5 cm. of the mitral ring. The ventricular wall at the site of infarction was 2 to 3 mm. thick and covered in its upper part

by pale laminated thrombus; in its lower part there was an interventricular communication measuring 1·5 cm. in its vertical axis and 0·8 cm. wide (Fig. 3). The endocardium on the right side of the septum was opaque and thickened for a distance of 1 cm. around the perforation. Both coronary arteries showed severe atheroma with numerous yellow crescentic plaques reducing the lumen to a mere slit-like space in areas. The right coronary, 2 cm. from its origin, was occluded for a distance of 1 cm. by an organized thrombus. The aorta showed severe atheroma and ulceration.

FIG. 3—Case 2. Left ventricular aspect. Infarct of septum with probe in large perforation.

Case 3. A man, aged 63, was admitted to the hospital in May, 1950. He had been well until ten days beforehand, when he complained of continuous pain in the front of the chest; but he was still able to carry on with his work. When seen, there were no cardiac murmurs. On the day he was admitted to the hospital he awoke with severe retrosternal pain and was very breathless. He was orthopnœic, apprehensive and his skin was pale and moist. His pulse rate was 100 a minute and regular in rhythm. The blood pressure was 90/75. The apex beat was faintly felt 11 cm. from the midline in the fourth left interspace. A systolic thrill was present to the left of the lower end of the sternum extending outwards to the apex. A harsh loud systolic murmur was heard all over the præcordium, and was loudest in the fourth interspace to the left of the sternum and at the apex.

The cardiogram showed prominent Q waves and S–T elevation in the limb leads and in CR1 and CR4.

He developed signs of heart failure. On the day after admission a pericardial rub was heard all over the sternum. Radiological examination of the chest showed a marked increase in the size of both sides of the heart with congestion at the lung bases. He died 14 days after the rupture of the interventricular septum.

Necropsy (Dr. A. G. Heppleston). The heart weighed 450 g. There was a fairly recent infarct involving the anterior part of the left ventricle and interventricular septum. The left ventricle was dilated. There was a perforation 0·5 × 0·5 cm. in the lower end of the interventricular septum. The pericardium showed fibrinous pericarditis with early organization. The valves were normal. There was thrombosis on the endocardium over the infarct. The coronary arteries were atheromatous; this was severe in the left descending branch which showed a recanalized thrombus. The aorta was atheromatous.

Discussion

Our three patients gave a history of recent cardiac infarction. At the start of the illness cardiac murmurs were not heard. Subsequently they complained of sudden severe pain in the epigastrium or in the chest accompanied by breathlessness. In these cases the clinical diagnosis of rupture of the interventricular

septum was made from the appearance of a harsh systolic mumur, perhaps with a systolic thrill, in the fourth or fifth interspace near the left border of the sternum. In our series the rupture was relatively small in Cases 1 and 3 and in these a thrill was palpable, but in case 2 only a systolic murmur was heard, where a large septal perforation was present. Reviewing the recorded cases it would seem that a systolic thrill is present if the perforation is small. The characteristic systolic murmur of an interventricular septal defect is usually situated in the fourth interspace near the left border of the sternum, but it is interesting to note that in Case 1 the thrill and the site of the maximum intensity of the murmur were gradually displaced laterally during the long period of observation. In accord with previous reports, all our patient's developed signs of heart failure immediately or very soon after the perforation of the septum. The clinical features of perforation of interventricular septum are almost identical in all the reported cases, but up to 1950 there have been three cases in which no murmurs have been noted and in these a clinical diagnosis was impossible. The only condition in any patient known to have had a cardiac infarction likely to be confused with septal perforation is rupture of a papillary muscle; this is even less common, the murmurs are louder, may be systolic and diastolic in time and nearer the apex of the heart. Cardiac failure is predominantly left sided.

It has been stated (MacWilliam, 1923) that the blood pressure can, under certain circumstances, be increased during sleep and this may explain the occurrence of the septal rupture during the night in our three cases. Disturbance of intraventricular conduction is very rarely found in cases of acquired septal perforation, and was not demonstrated in the electrocardiograms of our patients. Nareff *et al.* (1950) state that only three cases have been reported in which this defect of conduction has been noted. The rarity of this abnormality can be explained by the position of the perforation which is usually near the apex of the heart and this is shown in our specimens.

It is known that the interventricular septum is richly supplied by blood vessels and the infrequency of its rupture has been attributed to this adequate anastomosis. When perforation occurs there is usually severe and diffuse atheroma of the coronary arteries. In each of our patients, both coronary arteries were very atheromatous or actually occluded by a thrombus. Infarction of the septum is more often associated with infarction of the anterior wall of the left ventricle as in Cases 1 and 3 but less frequently, it is an extension of a lesion of the posterior wall as in Case 2.

In most of the recorded instances septal rupture has occurred within the first fortnight after the cardiac infarction and usually within the first week. In our patient's perforation of the septum took place after an interval of twenty-one days, twelve days and nine days respectively. Sager (1934) found that all those he reviewed died within ten days and Nareff *et al.* (1950) stated that, of all the reported cases, only seven lived for more than a month after the perforation. Wood and Livezey (1942) reported one patient who survived for four years and ten months, and it is noted that in this instance the interval between infarction and septal perforation was five weeks. One of our patients (Case 1) lived for eleven months and another (Case 2) for sixty-three days. In our experience it would seem that the longer the interval between the cardiac infarction and the occurrence of the rupture, the longer the duration of life after the septal perforation.

Conclusion

Three examples of perforation of the interventricular septum following a recent cardiac infarct are described and in all a diagnosis was made during life. The clinical and pathological features are discussed.

Perforation of the septum usually occurs within a fortnight of the initial cardiac infarction. Heart failure then develops and death usually ensues in less than one month from the septal perforation. One of our patients survived for eleven months.

We wish to thank Professor A. M. Kennedy for permission to publish Case 3, and Professor J. Gough for access to the necropsy records. We are indebted to Dr. William Evans for his helpful criticism and advice.

References

Fowler, N. O., and Failey, R. B. (1948). *Amer. J. med. Sci.*, **215**, 534.
Latham, P. M. (1845). *Lectures on Subjects connected with Clinical Medicine comprising Diseases of the Heart.* Longmans, Brown, Green and Longmans, London, **2**, 168.
MacWilliam, J. A. (1923). *Brit. med. J.*, **2**, 1196.
Nareff, M. J., Sklar, L. J., Kelly, F. T., and Reuling, J. R. (1950). *New Engl. J. Med.*, **243**, 431.
Sager, R. V. (1934). *Arch. intern. Med.*, **53**, 140.
Wood, F. C., and Livezey, M. M. (1942). *Amer. Heart J.*, **24**, 807.

PROCEEDINGS OF THE BRITISH CARDIAC SOCIETY

The THIRTY-FIRST ANNUAL GENERAL MEETING of the British Cardiac Society was held at the University, Western Bank, Sheffield, on Thursday, May 29, 1952. Chairman: J. W. BROWN. The Chairman took the Chair at 9.30 a.m.; 115 members and 13 visitors were present.

PRIVATE BUSINESS

1. The minutes of the last Annual General Meeting, having been published in the Journal (**13**, 569, 1951) were taken as read and confirmed.

2. The balance sheet for 1951–52 was presented, having been audited and found correct by H. Cookson and I. G. W. Hill. The credit balance on May 5 was £179 11*s.* 2*d.*

3. John Hay was elected and acclaimed as an Honorary Member of the Society.

4. W. M. Arnott and E. Wyn Jones were elected members of the Council in place of H. Cookson and I. G. W. Hill (terms of office expired).

5. The following Associate Members were elected as *Ordinary Members:*

R. E. Bonham-Carter	R. Kauntze	W. A. Oliver
E. M. Buzzard	G. A. Kiloh	D. A. Robertson
R. Daley	G. L. S. Konstam	R. W. D. Turner
D. H. Davies	A. Leatham	
Courtenay Evans	J. W. Litchfield	

6. The following *Associate Members* were elected for a further period of three years:

J. Benn	R. Kempthorne	D. Lewes
W. Stokes	A. J. Thomas	B. G. Wells

7. The following new *Associate Members* were elected and introduced:

R. I. S. Bayliss, London	J. D. Hay, Liverpool
A. J. V. Cameron, Glasgow	B. B. Hosford, Tunbridge Wells
J. A. Cosh, Bristol	J. F. Pantridge, Belfast
A. R. R. Cumming, Hull	E. G. Wade, Manchester
K. W. Donald, Birmingham	

8. The Society discussed the report on the reconstitution of the British Cardiac Society, which had been submitted to the Council by a sub-committee set up to consider an analysis of the questionnaire that had previously been sent out to all members. The sub-committee consisted of Sir John Parkinson, Dr. Evan Bedford, Dr. Maurice Campbell (Chairman), Dr. Shirley Smith, and Dr. Samuel Oram (Secretary). After a full discussion the following new rules were agreed to:

Previous Rule 5. Ordinary Members shall be Physicians or others whose primary interest is in the practice of Cardiology or in research in this or allied subjects.

Revised version. Ordinary Members shall be Physicians on the consultant staff of a hospital or others whose primary interest is in the practice of Cardiology or in research in this or allied subjects.

Previous Rule 6. Ordinary Members shall not exceed 75 in number and not more than 5 shall be elected annually. In addition there may be 10 Ordinary Members who may be elected for their interest in Cardiovascular Surgery.

Revised version. Ordinary and Associate Members shall not exceed 225 in number. This includes up to 15 Ordinary Members who may be elected for their interest in Cardiovascular Surgery.

Previous Rule 7. Extra-Ordinary Members shall not exceed 20 in number; they may be elected annually from among the senior Ordinary Members. For this purpose the Council may nominate

not more than 4 members to be proposed at the Annual Meeting. The affirmative vote of two-thirds of the members voting shall be required for election.

Revised version. Extra-Ordinary Members shall not exceed 25 in number; they may be elected annually from among the senior Ordinary Members. The affirmative vote of two-thirds of the members voting shall be required for election.

Previous Rule 9. Associate Members shall be elected from those engaged in research in cardiovascular problems or in the practice of Cardiology. Their number shall not exceed 50, and not more than 20 (including those re-elected) shall be elected in any year. The procedure for proposal and election of Associate Members shall be the same as for Ordinary Members.

Revised version. Associate Members shall be elected from those engaged in research in cardiovascular problems or in the practice of Cardiology. Their number, added to those of the Ordinary Members, shall not exceed 225, and not more than 15 new Associate Members shall be elected in any year.

Previous Rule 11. All Ordinary and Associate Members shall become subscribers to the Journal. (The subscription is 30*s.* per annum, reduced to 25*s.* for those who are members of the B.M.A.)

Revised version. All Ordinary and Associate Members shall become subscribers to the Journal. (The subscription is 42*s.* per annum.)

Previous Rule 21. The business of the Society shall be conducted by a Council which shall arrange the programme of each meeting. The Council shall consist of eight Ordinary Members and, in addition, the Chairman, the Chairman-Elect, the Editors of the Journal, and the Secretary. Two of the eight Ordinary Members shall retire annually in rotation and shall not be eligible for re-election for a period of one year. The Society shall elect two new members to serve in their place, and the Council may submit names for the vacancies.

Revised version. The business of the Society shall be conducted by a Council which shall arrange the programme of each meeting. The Council shall consist of eight Ordinary Members and, in addition, the Chairman, the Chairman-Elect, the Editor of the Journal or one of the Associate Editors delegated by the Editor to act as his deputy, and the Secretary. Two of the eight Ordinary Members shall retire annually in rotation and shall not be eligible for re-election for a period of one year. The Society shall elect two new members to serve in their place, and the Council may submit names for the vacancies.

Finally, an *additional rule* of the Society was agreed, namely, "There shall be a President of the Society who shall be elected by the Council."*

9. It was agreed to raise the *annual subscription* to two pounds for Ordinary Members and one pound, ten shillings for Associate Members. This alteration necessitates modifying Rule 22 of the Society which will now read: "The subscription shall be fixed by the Council and shall become payable on the first day of March. For Ordinary Members it is two pounds and for Associate Members, one pound, ten shillings. Failure to pay the subscription due within two years shall be considered equivalent to resignation."

Short Communications

A Study of Coronary and Myocardial Lesions

P. J. D. Snow (*introduced*), A. Morgan Jones and K. Daber (*introduced*). The coronary injection technique of Schlesinger (*Amer. Heart J.*, **15**, 528, 1938), combined with the serial slice method of myocardial examination has been used to examine 180 hearts. The first 25 cases of coronary disease have been analysed, 42 occlusions and 59 infarcts being present. This contrasts with the results of Blumgart, Schlesinger, and Davis (*Amer. Heart J.*, **1**, 19, 1940), who in 30 cases found 53 main-vessel occlusions and only 16 infarcts. Incomplete myocardial examination is the probable explanation for the small number of infarcts found.

In 10 cases a single occlusion resulted in an infarct that subsequently extended on one or more occasions without further occlusion. In another 3 cases a single occlusion was responsible for two anatomically separate infarcts. In all 13 cases the additional infarcts occurred in zones rendered ischæmic by the original occlusion. The period during which further infarction is most likely to occur is up to eight weeks.

Of 42 occlusions, all but 4 were followed by infarction, and in each of these 4, the occlusion was one of two in the same vessel.

All 18 old occlusions found had recanalized, and their functional significance is shown by the fact that re-occlusion in five was followed by fresh infarction in each case.

* The exact method of his election is being discussed further by the Council.

The rate of revascularization of infarcts was studied by the filling of the infarct with injection medium. This was complete in eight weeks, thus agreeing well with the traditional period of rest and with the time during which further infarction is liable to occur.

Electrocardiographic assessment of Posterior Cardiac Infarction

By Cornelio Papp and K. Shirley Smith. In a consecutive series of 100 patients with posterior cardiac infarction assessed according to severity of the attack, 22 per cent were slight, 21 per cent moderate, and 57 per cent severe. This was in contrast to anterior cardiac infarction where this incidence was 42 23, and 35 per cent respectively. Greater gravity in posterior infarction can be explained by the frequency of arrhythmias and by the tendency of some slight posterior infarctions to become severe, a development exceptional in slight anterior infarction.

In slight posterior cardiac infarction the following electrocardiographic patterns were shown: absent pathological Q waves in about half the cases; R–T and T changes of the subacute type, e.g. bowed R–T with isoelectric take-off and deep inversion of T; electrocardiographic restoration in about a quarter of the cases. The severe cases in contrast exhibited pathological Q waves in almost every instance, an acute pattern, e.g. high R–T take-off and monophasic T wave in the great majority, and arrhythmias in more than one-third of the cases. In the moderate group the incidence of these signs was transitional, except that no arrhythmias were observed. There was no mortality in the slight and moderate group during the first two months. The mortality in the severe group of treated and untreated cases was 33 per cent.

The diagnostic difficulties in slight posterior cardiac infarction were solved by effort test; IIIR and aVFR leads. Recent bipolar leads advised for posterior infarction proved disappointing. No diagnostic problems have arisen in the moderate and severe cases. The absence of secondary T wave changes in anterior chest leads proved an important point in the diagnosis of antero-posterior cardiac infaction.

In five patients slight cardiac infarction was followed by increasingly severe angina; two of these developed severe posterior cardiac infarction within a fortnight, and one of them died. Early anticoagulant treatment delayed the severe attack by months in one, while in the other two it prevented it. All five showed the electrocardiographic signs of posterior subendocardial infarction consisting in sagging or flat R–T depression in leads II, III and VF. Effort test caused temporary subepicardial ischæmia and this result was considered an important indication for prompt anticoagulant treatment.

The Heparin-Retarded Coagulation Time in Coronary Occlusion

By A. A. F. Peel. To be published in full, *Brit. Heart J.*, 1953.

Ischæmic Heart Disease and Peripheral Occlusive Arterial Disease

By Lawson McDonald. This paper gives the results of a study made during the past two years of patients with occlusive arterial disease, either resulting in ischæmic heart disease or affecting the blood supply to the legs. An attempt is made to estimate how often the two conditions occur together.

Eighty-seven patients presenting with intermittent claudication due to occlusive arterial disease have been examined clinically, and also by arteriography, tonoscillography after exercise, cardioscopy, and unipolar lead electrocardiography. Nearly half of these patients had evidence of ischæmic heart disease. Fifty patients presenting with angina pectoris due to occlusive coronary arterial disease have also been examined; in about a quarter evidence was found of occlusive arterial disease affecting the blood supply to the legs.

The coincidence of ischæmic heart disease and occlusive arterial disease affecting the legs is shown to be high. Although the clinical association of these two conditions, manifested by angina pectoris and intermittent claudication, is well recognized, there is scanty information regarding the frequency of their coincidence. The findings in these cases are particularly analysed with regard to sex, blood pressure, the age of onset and the duration of symptoms; the three groups are compared. In deciding upon treatment, either medical or surgical, for these patients, the importance of a knowledge of the coexistence of the other condition is noted.

The Diagnosis of Phæochromocytoma

By W. S. Peart (*introduced*) and J. W. Litchfield. The various methods of diagnosis are considered with reference to their use in 5 patients. The common features of pallor, palpitations, headache, vomiting,

breathlessness, and hypertension are stressed, while attention is drawn to some rarer symptoms and signs, such as swelling of the thyroid and A-V dissociation. Although the hypertension is commonly paroxysmal, three cases with fluctuating sustained hypertension were seen. The type of case with maintained steady hypertension is probably rare. There were two cases with malignant hypertension as judged by retinal changes, though no fibrinoid arteriolar necroses were discovered in the suprarenals. Localization of the tumours when not palpable has been accomplished by repeated soft tissue radiographs or pyelography. The blood flow through the hand was low in all except one of these patients, even when the blood pressure was normal, and this suggests that the pressor substances were released continually. Pharmacological methods of diagnosis, involving the use of stimulating drugs like histamine or antagonist drugs like benzodioxane, have been misleading in cases reported elsewhere, and two false negative tests with benzodioxane occurred here. The best method was the estimation of the urinary excretion of adrenaline and nor-adrenaline described by Euler and Engel. An increased excretion was found in all our cases.

Rapid Methods of Assessing Heart Failure

By E. P. Sharpey-Schafer. Postural changes in peripheral blood flow and arterial pulse pressure showed conspicuous differences in normal subjects and subjects with heart failure. Similar differences in the circulation have been found during and following the Valsalva manœuvre and the mechanisms involved have been investigated. The Valsalva manœuvre may be used as a simple clinical test.

Cardiac Output in Man

By J. McMichael. A film of this was shown at the end of the morning session.

Clinical Value of the A Wave of the Jugular Pulse

By Paul Wood. A film of this was shown at the opening of the afternoon session.

Pulmonary Artery and Pulmonary Capillary Pressures in Mitral Stenosis, and their Response to Exercise

By F. Jackson. The resting mean pulmonary artery, pulmonary capillary, and right ventricular pressures were measured by means of saline manometer in 50 cases of mitral stenosis.

The relation between the pulmonary artery and capillary pressures was in simple proportion at the lower levels, but the arterial pressure rose disproportionately when the capillary pressure exceeded 30–35 cm. saline, as described by Dexter *et al.* (*J. Clin. Invest.*, **29**, 602, 1950) and by H. E. Holling (*Guy's Hosp. Gaz.*, **65**, 271, 1951). The mean pulmonary artery and right ventricular pressures showed a linear relationship except at high levels. Clinical estimation of the severity of pulmonary hypertension based on the symptoms, signs, and radiological and electrocardiographic findings correlated reasonably well with the measured pressures.

In 9 patients re-catheterized between 3 and 12 months after valvulotomy the resting pulmonary artery and pulmonary capillary pressures were lower than before operation. In very severe cases, however, the artery pressure did not fall commensurately with the capillary pressure, possibly because of secondary vascular changes in the lungs.

Exercise produced a substantial rise in both pulmonary artery and capillary pressures followed by a slow fall to the resting level, even in the slighter grades of stenosis, compared with a small rise and rapid fall in controls without pulmonary hypertension. The actual increase in pressure was not a reliable index of the degree of stenosis, and the rate of the subsequent fall seemed to be a better guide.

Comparison with the artery and capillary pressures in pulmonary hypertension from other causes shows that the resting *pulmonary capillary* pressure relates more closely to the degree of mitral stenosis than does the *pulmonary artery* pressure, and it probably affords a better measure of the success of operation.

Observations on Pulmonary Circulatory Physiology in Mitral Valve Disease

By Geoffrey Wade, Lars Werkö, and Harald Eliasch (*introduced by Crighton Bramwell*). Using the basic technique of cardiac catheterization 26 cases of mitral disease were studied at rest and after a period of graded work. The measurements made in each case were the cardiac output, the pulmonary

arterial and capillary pressures, the pulmonary arteriolar resistance, and the cardio-pulmonary blood volume.

Results. It was found that there was an inverse relation between the cardiac output and the pulmonary capillary pressure and that a rise in this pressure on effort was generally accompanied by an increase in the pulmonary blood volume. A similar inverse relation existed between the output and the pulmonary arterial pressure but this was curvilinear owing to the frequent occurrence, in the more severe cases, of an increase in the degree of pulmonary arteriolar resistance leading to higher pulmonary arterial pressures. In these " high resistance " cases there was a smaller increase in the pulmonary blood volume in relation to the degree of pulmonary arterial pressure rise. The effect of high arteriolar resistance, which by shielding the capillaries from the output of the right ventricle may act as a useful barrier, is demonstrated. The modifying effects of the development of right heart failure on the pressure-flow pattern is also pointed out.

The nature of the increase in pulmonary resistance is discussed and its rapid reversability after successful mitral valvulotomy is shown.

The Oesophageal Pulse in the Diagnosis of Mitral Incompetence

By Max Zoob (*introduced by Frances Gardner*). Incompetence of the mitral valve is expected to produce abnormal filling of the left auricle and consequently abnormal movements of the contiguous portion of the œsophagus.

A study of the œsophageal pulse has, therefore, been made in the hope of facilitating the diagnosis of mitral incompetence. A duodenal tube was adapted to permit the simultaneous registration of the œsophageal pulse and electrocardiogram. The tube could be passed through the nose with little disturbance to the patient. The position of the recording tip—with reference to the left auricle—was determined from the contour of the P wave of the œsophageal electrocardiogram as well as by fluoroscopy. A conventional phonocardiogram was recorded simultaneously as an additional reference tracing.

Thirty-five control subjects in whom there was no suspicion of mitral valve disease were studied. These included patients with hypertensive heart disease or aortic valve disease and normal subjects. All showed essentially similar records. At auricular levels, a, c, and v waves were found analogous to those of jugular phlebogram. The summit of the v wave never preceded the second heart sound. Nine subjects thought to have innocent apical systolic murmurs showed similar curves.

Six patients thought to have pure mitral incompetence were studied. All showed striking abnormalities of the œsophageal pulse at auricular levels. The upstroke of the v wave was abnormally abrupt and its summit occurred before the second heart sound. This curve was thought to be due to abnormal auricular filling consequent upon mitral incompetence.

Fourteen of thirty-nine patients with mitral stenosis showed somewhat similar abnormalities. As, however, the curves were not identical with those found in pure mitral incompetence and as many of the patients showed no clinical or radiological evidence of incompetence, other modes of production of such abnormal curves are considered.

It is therefore concluded, that although an abnormal auricular filling wave cannot at present be used as evidence of incompetence in cases of mitral stenosis, it nevertheless provides evidence of mitral valve disease in subjects without diastolic murmurs.

Valvulotomy in Congenital Mitral Stenosis

By A. L. d'Abreu and Clifford Parsons. Congenital mitral stenosis is of two types. The first probably results from unequal division of the common atrio-ventricular canal and the second is due to an abnormality, possibly endocarditis, occurring later in fœtal life. Surgery would be impossible in the first type as there is always hypoplasia of the left ventricle and aorta. In the second variety hypoplasia is not necessarily severe, myocardial involvement is slight and obstruction at the thickened, narrow mitral valve is the essential cause of disability and invites surgical relief.

Our patient was referred because of repeated attacks of bronchitis, pneumonia, and congestive heart failure; she had had no illness suggestive of acute rheumatism. Her eldest brother had a patent ductus arteriosus but no member of the family had had rheumatic fever. Her mother's pregnancy had been normal. The new born infant was said to have signs of congenital heart disease and when we first examined her at the age of three and a half she had classical mitral stenosis. Investigations showed large P waves and right ventricular preponderance; congested vessels, slight general cardiac enlargement, but not particularly the left auricle on fluoroscopy; a patent ductus arteriosus with reversed flow on angiocardio-

graphy; and evidence of an intact septum, and raised pressure and oxygen content in the pulmonary artery on cardiac catheterization.

The child's condition deteriorated in the next year. With increasing frequency her feet were observed to be bluer than her hands.

At the age of four and a half her thorax was explored. Temporary occlusion of the ductus did not abolish the apical murmurs nor reduce the pulmonary artery pressure (145 cm. of saline). The distended left auricle was opened and the mitral valve felt as a hard fibrotic diaphragm, with a central aperture but no commissures. With great difficulty it was dilated until the index finger passed easily, but splitting of the valve could not be achieved. After operation there was temporary improvement, but within two weeks pulmonary hypertension was again sufficient to cause persistent slight cyanosis of the lower half of the body.

It is concluded that, owing to the nature of the valve deformity in congenital mitral stenosis, digital dilatation is unlikely to relieve the obstruction.

The Anatomy of Pulmonary Stenosis

By J. W. A. Duckworth (*introduced*) and R. M. Marquis. The developmental changes occurring in the bulbo-ventricular region of the human heart from the fifth to the eighth week of intra-uterine life are compared with the anatomical features found in congenital malformations of the heart in order to show the probable time of action of the factors that result in such defects.

The relationship of these defects to dextroposition of the aorta, pulmonary stenosis, and patent interventricular foramen is discussed.

The principal sites of the stenosis included under the general heading of pulmonary stenosis are (1) the infundibulo-ventricular junction, (2) the infundibulum, (3) the pulmonary valves, and (4) the trunk of the pulmonary artery. More than one type may occur in the same patient and they may or may not be associated with other cardiac abnormalities.

Once stenosis has been established the resulting changes in the anatomy of the adult heart are noted and shown to depend chiefly on the degree of stenosis and the presence or absence of other cardiac abnormalities.

Patent Ductus Arteriosus with Pulmonary Hypertension

By J. A. Cosh. Three patients with patent ductus arteriosus are described in whom the pulmonary artery pressure was approximately equal to the aortic pressure. None had a continuous murmur, but the diagnosis in all was proved by the passage of a cardiac catheter along the ductus into the aorta. In two, the usual blood flow appeared to be from pulmonary artery into aorta. In the third, the flow was from aorta into pulmonary artery, but there was in addition coarctation of the aorta; this was confirmed by thoracotomy with lung biopsy. In none was the ductus ligated.

The clinical diagnosis and the relationship to simple patency of the ductus arteriosus are discussed.

Effort Syncope in Primary Pulmonary Hypertension and Fallot's Tetralogy

By Shiela Howarth and J. B. Lowe. Blood pressure records have been obtained in cases of primary pulmonary hypertension and Fallot's tetralogy, in which exercise produced loss of consciousness. The fall in systemic blood pressure leading to syncope occurred after exercise and was gradual and not precipitous. In one case of Fallot's tetralogy, loss of consciousness occurred five minutes after the end of exercise. Sinus bradycardia occurred when the blood pressure had fallen to low levels.

One case of primary pulmonary hypertension was exercised during cardiac catheterization and lost consciousness while lying supine on the couch. Pulmonary arterial pressure and blood pressure rose during feet exercise. At the end of exercise, the systemic blood pressure fell, the pulse pressure in the right ventricle decreased, and the diastolic pressure in the ventricle rose. These results are compatible with acute failure of the right ventricle from increased stress.

EUROPEAN CONGRESS OF CARDIOLOGY

The first European Congress of Cardiology was held on September 9–12, 1952, in the University of London. It was organized by the British Cardiac Society on behalf of the European Society of Cardiology.

Honorary President	Prof. CHARLES LAUBRY (*Paris*)
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OPENING OF CONGRESS

September 10, 1952

Sir John Parkinson, Chairman of the Congress and President of the British Cardiac Society, welcomed Members of the Congress.

Professor Charles Laubry, Honorary President of the European Society of Cardiology, addressed the assembly.

Professor Gustav Nylin, President of the European Society of Cardiology, gave an address and declared the Congress open.

Programme of Scientific Sessions

Wednesday, September 10. Morning: Beveridge Hall

Coronary Artery Disease

Joseph Lambert (*Spa, Belgium*). Value of additional unipolar leads for the diagnosis of localization and extension of myocardial infarctions.

William Evans (*London*). The electrocardiogram in 1000 patients with cardiac infarction.

Irving S. Wright (*New York*). An evaluation of the anticoagulants.

P. J. D. Snow, A. Morgan Jones, and K. Daber (*Manchester*). A study of coronary and myocardial lesions.

E. Coelho, J. M. Fonseca, C. Rocha Pinto, and A. Nunes (*Lisbon*). Coronary arteriography in the living subject and its importance for the study of anastomoses of the coronary arteries.

Wednesday, September 10. Morning: Assembly Hall

Congenital Heart Disease

J. F. Goodwin and A. Pagnoni (*London*). Cardiographic diagnosis of combined ventricular hypertrophy.

J. Laham, C. Metianu, M. Durand, and G. Dauzier (*Paris*). Electrocardiographic study of combined ventricular hypertrophy in congenital heart disease.

J. Dankmeijer and J. Los (*Leiden*). Embryology of the pulmonary veins.

J. Lequime, F. Courtoy, H. Denolin, and J. Kenis (*Brussels*). Hæmodynamics in isolated ventricular septal defect.

Ruby M. Collister, J. Dankmeijer, and H. A. Snellen (*Leiden*). Vascular changes in the collateral lung-circulation in severe pulmonary stenosis and atresia.

C. Metianu, M. Durand, and T. Doliopoulos (*Paris*). The significance of a negative P wave in lead I in congenital heart disease.

Maurice Campbell and Geoffrey Reynolds (*London*). The significance of the direction of PI in dextrocardia and isolated lævocardia.

Wednesday, September 10. Afternoon: Beveridge Hall

Congenital Heart Disease

J. Lind and C. Wegelius (*Stockholm*). Changes in the human circulation at birth. An angiocardiographic study.

H. Lichtenstein, J. Lind, and C. Wegelius (*Stockholm*). Angiocardiography in experimental heart disease.

E. Donzelot, R. Heim de Balsac, C. Metianu, M. Durand, and R. Guillemot (*Paris*). Radiological study of 400 cases and anotomical and radiological comparison of 60 necropsies of tetralogy of Fallot.

C. Metianu, M. Durand, J. Laham, and G. Dauzier (*Paris*). Electrocardiographic study of 32 cases of pulmonary stenosis with intact ventricular septum.

G. Jonsson, B. Broden, and J. Karnell (*Stockholm*). Selective visualization of pulmonary stenosis.

A. G. Brom (*Holland*). The value of valvotomy in pure pulmonary stenosis and in pulmonary stenosis combined with over-riding aorta.

J. Karnell (*Stockholm*). Surgical treatment of coarctation of the aorta.

F. d'Allaines, N. du Bouchet, and B. I. Latscha (*Paris*). Hexamethonium during operations for stenosis of the aortic isthmus.

C. C. Maggi and F. Seitun (*Milan*). Clinical, radiological, and tomographical study of the rare forms of stenosis of the thoracic aorta.

Wednesday, September 10. *Afternoon: Assembly Hall*

ELECTROCARDIOGRAPHY

Jean Lenègre and Henri Chevalier (*Paris*). Correlation of electrocardiograms with lesions of the Tawara-His system of A-V block and bundle branch block, and ventricular hypertrophy.

Fr. Van Dooren and N. Boyadjian (*Brussels*). Configuration of the QRS complexes in A-V block.

L. Cabral (*Lisbon*). S-waves in intraventricular block.

R. Hegglin, H. Grauer, and A. Munchinger (*Zurich*). Experimental investigations on the cause of Q-T prolongation.

V. Brossa Torres (*Barcelona*). The clinical value of monopolar leads.

P. Rijlant (*Brussels*). Polygraphic exploration of the distribution of cardiac potentials on the surface of the thorax.

S. Caccuri and G. Grazziani (*Naples*). The ventricular gradient in bundle branch block.

J. Varela de Seijas Aguilar, E. Uriel Morales, and H. Herrero Botas (*San Rafael*). The ventricular gradient with reference to the repolarization process.

M. Corti and V. Macchi (*Milan*). Electrocardiograms known as " of overload " following changes in the intracavitary pressures after surgical treatment.

Thursday, September 11. *Morning: Beveridge Hall*

SYMPOSIUM ON THE SURGICAL TREATMENT OF MITRAL STENOSIS

Opening Speakers

Maurice Campbell (*London*). P. Soulié (*Paris*). L. Werkö (*Stockholm*). R. Froment (*Lyons*). Paul Wood (*London*).

Followed by

T. Holmes Sellors (*London*). P. Santy (*Lyons*). C. Crafoord (*Stockholm*). A. M. Dogliotti (*Turin*). H. A. Snellen (*Holland*). G. A. Mason and W. G. A. Swan (*Newcastle*). O. Branko (*Yugoslavia*). Erik Warburg (*Copenhagen*).

Thursday, September 11. *Afternoon: MacMillan Hall*

FURTHER PAPERS ON THE SURGICAL TREATMENT OF MITRAL STENOSIS

W. Bolt and H. Venrath (*Germany*). Functional analysis with special reference to surgical treatment of mitral stenosis.

V. Puddu, L. Comberiati, A. Collicelli, and A. Sensi (*Rome*). Electrocardiographic, phonocardiographic, and electrokymographic changes in mitral stenosis after commissurotomy.

A. Cordeiro and E. Lima Basto (*Lisbon*). Post-operative course of mitral valvotomy.

F. S. P. van Buchem, J. Nieveen, B. P. A. A. Homan, and W. E. Marring (*Holland*). Some observations on patients operated on for mitral stenosis.

L. Condorelli (*Rome*). The regulator mechanisms of pulmonary arterial pressure.

M. Servelle (*Paris*). Experimental study of mitral valvoplasty: hæmodynamics and results.

F. Jackson (*Newcastle*). Pulmonary artery and pulmonary capillary pressures in mitral stenosis, and their response to exercise.

H. A. Snellen, J. Dankmeijer, P. H. M. Schilling, J. Van Dam, H. G. Verdonk (*Holland*). Clinical significance of biopsies from the left lung and left auricle in mitral stenosis.

Thursday, September 11. *Afternoon: Beveridge Hall*

MISCELLANEOUS SUBJECTS

G. Nylin and G. Hevesey (*Stockholm*). Application of Thorium B. labelled red corpuscles in the determination of the blood volume.
G. W. Pickering, M. Hamilton, and G. S. C. Sowry (*London*). The inheritance of benign essential hypertension.
H. Welti and C. Lian (*Paris*). The treatment of essential hypertension by an arterio-venous fistula.
F. Lenzi and A. Caniggia (*Siena*). Experiments on the osmodynamic energy accumulator theory.
R. Daley and I. McMillan (*London*). The heart beat in the dog as shown by high speed cinematography.
J. Lequime, P. Courtoy, and J. Kenis (*Brussels*). Hæmodynamics in combined left and right ventricular failure.
A. Poppi, G. Labo, and G. Lenzi (*Bologna*). Liver and pancreas function in heart disease.
L. Gallavardin, R. Froment, and P. Cahen (*Lyon*). Benign forms of paroxysmal ventricular tachycardia.

Thursday, September 11. *Afternoon: Assembly Hall*

MAINLY ELECTROCARDIOGRAPHY AND VECTORCARDIOGRAPHY

A. de Sousa Pereira (*Oporto*). Superior cervical sympathectomy and ligation of external carotid artery in the treatment of cerebral vascular diseases.
M. Iverson (*Copenhagen*). Heart disease and prostatic surgery.
G. Agostoni (*Milan*). The zone of the aortic isthmus " locus minoris resistentiæ " in cases of violent trauma of the chest.
V. Slavkovic (*Yugoslavia*). Clinical significance of aVR leads in which the main QRS deflection is upward.
J. Gibert-Queraltö, M. Torner-Soler, J. Paravisini, and J. M. Morato-Portell (*Barcelona*). The physiogenesis of the left intracavitary electrocardiogram.
P. Meyer, R. Herr, Cl. Schmidt, P. Millian (*Strasbourg*). Unipolar dorsal leads, especially V8 and Inf. 8 in electrocardiography.
M. Segers (*Brussels*). Preponderance considered as an intraventricular block.
M. Regnier and B. Taccardi (*Belgium*). The frontal vectorcardiogram in man.
R. Wenger (*Vienna*). The vectorcardiographic investigations in incomplete bundle branch block.
R. Ivancic (*Zagreb*). Transthoracic bipolar leads.
J. Shillingford and W. Brigden (*London*). The vectorcardiogram in mitral stenosis.

Friday, September 12. *Morning: Beveridge Hall*

MITRAL STENOSIS AND MITRAL INCOMPETENCE

G. Biörck, O. Axen, H. Krook, L. Andren, and H. B. Wulff (*Stockholm*). The relative merits of various diagnostic methods in mitral valvular disease.
H. E. Holling and A. Venner (*London*). The diagnosis of mitral incompetence.
W. Brigden and A. Leatham (*London*). Mitral incompetence.
S. R. Kjellberg, U. Rudhe, H. Eliasch, and L. Werkö (*Stockholm*). Evidence for left auricular contraction and mitral regurgitation in mitral valvular disease.
R. Turner (*Edinburgh*). The surgical treatment of mitral incompetence.

P. F. Angelino and A. Actis-Dato (*Milan and Turin*). Angiocardiopneumography in mitral stenosis.
J. Facquet, J. M. Lemoine, P. Alhomme, and G. Lefebvre (*Carnot*). The measurement of the left auricular pressure through the bronchus.
I. Mahaim, P. Desbaillets, and J. Wyss (*Lausanne*). The mitral stenosing left auricular polyp and commissurotomy: a new symptom.

Friday, September 12. *Morning: Assembly Hall*

BALLISTOCARDIOGRAPHY, ELECTROKYMOGRAPHY, AND MISCELLANEOUS SUBJECTS

H. Burger (*Utrecht*). The physical principles of ballistocardiography.
L. Jonnart and J. Lequime (*Brussels*). Ballistocardiography from the physical standpoint.
R. Boehmig (*Karlsruhe*). Morphological development of the different types of endocarditis.
E. Donzelot and J. E. Escalle (*Paris*). Bacteriology and treatment of subacute bacterial endocarditis (Osler's disease).
R. Scalabrino (*Milan*). Subacute bacterial endocarditis with positive and negative blood culture, and its treatment.
A. Gonin, R. Froment, and J. Gravier (*Lyons*). Tuberculous pericarditis progressing to constrictive pericarditis.
F. Estape (*Barcelona*). Mitral destruction without valvular disease in constrictive pericarditis.
J. Paravisini-Parra, J. Gibert-Queraltö, M. Torner-Soler, J. Moralto-Portell, and A. Gregorich-Serrat (*Barcelona*). The investigation of constrictive pericarditis before surgical treatment.
L. Trias de Bes and F. Ballesta Barcons (*Barcelona*). The tolerance to khellin.

Friday, September 12. *Afternoon: Beveridge Hall*

MISCELLANEOUS SUBJECTS

A. Juvenelle, J. Lind, and C. Wegelius (*Stockholm*). Experimental hypothermia and cardiac surgery. Observations with an extra-corporeal circulation at reduced body temperature.
K. Blumberger (*Dusseldorf*). The dynamics of mitral and aortic valve diseases.
G. Minot, C. Lian, Herbert, and Rager (*Paris*). Simultaneous registration of the electrical and mechanical phenomena of the heart and vessels.
A. Thomas (*Cardiff*). The vascular lesion of pneumoconiosis.
Evans Jones and I. McMillan (*London*). The movement of aortic and pulmonary valves studied post-mortem by colour cinematography.
V. Debenedetti (*Ivrea, Italy*). The lasting inversion or flattening of the T wave in pulmonary embolism.
K. E. Grewin (*Stockholm*). The normal electrocardiogram in pregnant women during the last trimester and after delivery.
M. Holzmann (*Zurich*). Influence of respiration upon arrhythmias.
J. Ulrich (*Germany*). Contribution to the physiology of the heart.

Friday, September 12. *Afternoon: Assembly Hall*

CORONARY DISEASE AND PERIPHERAL VASCULAR DISEASE

H. Malmros (*Sweden*). The relationship of diseases of the coronary arteries and of the gall bladder.
V. Lapiccirella and G. Weber (*Florence*). The localization of coronary and gastro-mesenteric arteriosclerosis with reference to associated gastro-mesenteric syndromes.
K. Shirley Smith and C. Papp (*London*). Electrocardiographic assessment of posterior cardiac infarction.

G. Michaelides, H. Tsevreni, and D. Avgoustakis (*Athens*). Observations on the treatment of cardiac infarction by means of anticoagulants.
E. Donzelot and H. Kaufman (*Paris*). Angina and heparin.
Y. Bouvrain, R. Tricot, P. Vernant, and P. Meudic (*France*). A study of the freezing point of serum and of azotemia in recent cardiac infarction.
P. Hedlund (*Stockholm*). The appearance of acute phase protein in myocardial infarction.
B. Ejrup (*Stockholm*). Fluorescin circulation rate in peripheral vascular diseases.
G. Bendiera (*Genoa*). The determination of functional damage in the estimate of the gravity and evolution of vessel diseases of lower limbs.

The Organizing Committee expresses its gratitude to the following firms which have generously contributed towards the expenses of the Congress:

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ABSTRACTS OF CARDIOLOGY

Procaine Amide (Pronestyl in the Treatment of Cardiac Arrhythmias. J. M. KINSMAN, W. R. HANSEN, and R. L. MCCLENDON. *Amer. J. med. Sci.*, **222**, 365–374, Oct., 1951.

Procaine amide (" pronestyl ") was injected intravenously at a rate of 100 mg. a minute and in a total dose of not more than 1 g. in 6 minutes to patients with various types of cardiac arrhythmia. Altogether 41 patients were treated.

In 22 patients with auricular fibrillation no effect was produced with the maximum dose, but in 2 cases of paroxysmal auricular fibrillation this reverted to sinus rhythm after injection of 300 mg. and 550 mg. respectively. There was no response to treatment in 2 patients with auricular flutter. In 2 of 4 patients with ventricular tachycardia the tachycardia stopped promptly; and ventricular extrasystoles were abolished in 12 of 14 patients, although they almost invariably returned in minutes, hours, or days. Subjective toxic effects were few and slight, but the peripheral blood pressure was always lowered, as was also the pulmonary blood pressure. The cardiac output was decreased and the circulation time increased, and there was a prolongation of intraventricular conduction time.

In view of the toxic effects it is recommended that intravenous procaine amide should be used only for patients with paroxysmal arrhythmia in immediate danger of death or when other measures have failed, or for patients under anaesthesia. *C. Bruce Perry*

The Use of Carboxylic Cation Exchange Resin in the Therapy of Congestive Heart Failure. A. W. FEINBERG and B. ROSENBERG. *Amer. Heart J.*, **42**, 698–709, Nov., 1951.

Case reports are given of patients treated with a resin mixture which exchanged both potassium and ammonium ions for sodium. By this means it was hoped to avoid the hyperpotassaemia and acidosis produced respectively by the two constituents when employed alone. Five patients with congestive cardiac failure appeared to benefit, the longest period of observation being more than 1 year. The dyspnœa and orthopnœa were relieved in these patients and less frequent use of mercurial diuretics became possible, although venous congestion and œdema were less strikingly improved. In a sixth patient with impaired renal function acidosis developed before his symptoms were relieved, and in another patient gastro-intestinal irritation prevented continuance of treatment. In a patient in the nephrotic stage of chronic glomerulonephritis no diuresis occurred.

The possible toxic effects of these resins are discussed, and the advantages of fewer injections, fewer visits to the clinic, and less rigid dietary sodium restriction are stressed. *Albert Venner*

Prolonged Cation-exchange Resin Therapy in Congestive Heart Failure. C. VOYLES and E. S. ORGAIN. *New Engl. J. Med.*, **245**, 808–811, Nov. 22, 1951.

Resodec is a carboxylated cation-exchange resin which is saturated with both ammonium and potassium ions. In the stomach these cations are exchanged for hydrogen ions; in the bowel the hydrogen ions are exchanged for sodium, potassium, and calcium ions. The powdered resin is given in doses of 15 g. 3 times daily in milk or mixed with food. Added calcium is given as calcium lactate, 5 g. daily, or as milk, 16 oz. (450 ml.) daily. Sufficient potassium is supplied in the saturated resin. There is, however, a risk of hypocalcæmia, hypopotassæmia, or acidosis developing; and weekly estimations of the serum calcium, potassium, chloride, and CO_2-combining power are advisable, as well as the 24-hourly determination of urinary excretion of sodium and chloride.

Three ambulatory patients suffering from chronic congestive failure were given the resin daily for from 5 to 9 months. Before treatment with the resin all were receiving mercurial diuretics twice weekly and were on a diet containing only 500 mg. of sodium. During resin therapy only occasional injections of mercurials were required and 1 patient was able to increase his intake of sodium to 1500 mg. daily. When the resin was discontinued temporarily, congestive failure returned rapidly. During resin therapy the 24-hour urinary excretion of sodium fell to about 15 mg., but the serum sodium, calcium, and CO_2-combining power showed low to normal values; the serum potassium remained normal. One patient had severe constipation. It is concluded that the administration of a cation-exchange resin is a useful adjunct to the treatment of chronic congestive heart failure. *C. W. C. Bain*

An Aortic Deformity Simulating Mediastinal Tumour: a Subclinical Form of Coarctation. C. R. SOUDERS, C. M. PEARSON, and H. D. ADAMS. *Dis. Chest.*, **20**, 35–45, July, 1951.

Three examples of an unusual aortic deformity are described. There were no clinical signs or symptoms. The deformity appeared in the postero-anterior chest radiograph as a mediastinal soft-tissue density overlying a normal aortic arch. Thoracotomy in one case showed that there was a kinking deformity of the aorta toward the pulmonary artery at the attachment of a short ductus arteriosus; minimal narrowing of the aorta was present. *Kenneth Marsh*

Vascular Spasm. G. W. PICKERING. *Lancet*, **2**, 845–850, Nov. 10, 1951.

The idea of severe and localized contraction of an artery, vascular spasm, occurring in the absence of a recognizable

stimulus is entertained too freely and uncritically in current thought and writing. When a large artery such as the femoral is occluded in a normal subject, the distal blood-flow drops to zero for a few minutes and then returns to normal while the occlusion is maintained. Examples are given of transient symptoms of ischæmia following organic arterial occlusion in disease. Many, though not all, of the alleged instances of vascular spasm occurring in limbs, eye, brain, and heart seem to be explicable on other grounds of which the chief is organic arterial occlusion.—[Author's summary.]

The Cardiovascular Response of Normal Young Adults to Exercise as Determined by the Double Master Two-step Test. C. B. THOMAS. *Bull. Johns Hopk. Hosp.*, **89**, 181–217, Sept., 1951.

The experimental work described in this paper deals with the cardiovascular response to standard exercise in 263 healthy young medical students. The investigation required the use of a modification of the Master test, described as the " double Master two-step test ", in which the subjects tested made twice the usual number of trips over the steps in twice the time. Observations of the changes in blood pressure, heart rate, and electrocardiogram (standard limb leads and CF4) were recorded immediately after cessation of exercise.

Great variations in the cardiovascular response were noted, but in general the same subject exhibited similar patterns of response on repetition of the experiment. A group of " hyperreactors " to the exercise test were singled out, and among them obesity, high resting blood pressure, transitory hypertension, high resting heart rate, transitory tachycardia, and a positive cold pressor response were more frequently encountered than among the rest of the subjects. Furthermore, the majority of these subjects had a family history of hypertension with or without coronary artery disease. Thus the concept of an individual constitutional hæmodynamic pattern of response to circulatory stress can be visualized, a pattern which " is as distinctive as the physiological characteristics observed under resting conditions, and which may be of greater significance in terms of future cardiovascular disease."

[This is a well-documented and balanced study on the subject and its publication will undoubtedly stimulate more investigations on similar lines.]

A. I. Suchett-Kaye

The Mechanism and Significance of the Cold Pressor Response. H. H. WOLFF. *Quart. J. Med.*, **20**, 261–273, July, 1951.

The degree of the rise in blood pressure as a result of immersion of a hand in ice-cold water was originally considered as providing a measure of the greater reactivity in this respect of subjects with established or potential essential hypertension, since the rise in blood pressure was found to be greater than in healthy subjects. This claim has not since been substantiated.

The present investigation was undertaken in order to clarify what determined the height of the cold pressor response and what significance, if any, can be attached to it. The pain experienced during the test was already recognized as an important factor to account for the response, but the question had to be clarified whether the afferent impulses responsible for the rise in blood pressure excited a vasomotor reflex at some level below that at which pain is perceived, or whether the perception of pain was a pre-requisite for the increase in blood pressure. Tests carried out in 3 patients with hemianæsthesia due to cerebral vascular lesions, 6 with hysterical anæsthesia, 2 with analgesia due to syringomyelia, and one with a peripheral-nerve lesion demonstrated that immersion of the anæsthetic limb did not cause any significant increase in blood pressure.

The importance of avoiding any rise in blood pressure due to emotional factors, such as apprehension in connexion with the test, is stressed. It is concluded that the vasoconstriction underlying the cold pressor response occurs only as a reaction to the pain experienced during the test and is not the result of a reflex. This test therefore provides a measure of an individual's sensitivity to pain, and its value lies in further research on this subject rather than in connexion with hypertension.

A. Schott

The Use of Quinidine in Established Auricular Fibrillation and Flutter. D. HOLZMAN and M. G. BROWN. *Amer. J. med. Sci.*, **222**, 644–652, Dec., 1951.

Of 57 patients with auricular fibrillation or flutter it was possible to establish normal sinus rhythm in 30, but in 14 this could be maintained only during a follow-up period of 6 months. It appears to the authors that long-standing arrhythmia, cardiac enlargement or rheumatic heart disease does not satisfactorily respond to quinidine, but that when such a response is obtained it is usually in patients who have been given moderate doses.

The dosage of quinidine used was 0·2 g. every 2 hours for 7 doses. If normal sinus rhythm was established a maintenance dose of 0·2 g. was given 6-hourly for a month and then discontinued. *James W. Brown*

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